09/582059

d his

(FILE 'HOME' ENTERED AT 18:46:06 ON 06 AUG 2002)

FILE 'REGISTRY' ENTERED AT 18:46:14 ON 06 AUG 2002
L1 STRUCTURE UPLOADED
L2 9 S L1
L3 STRUCTURE UPLOADED
L4 0 S L3
L5 0 S L4 SSS FULL

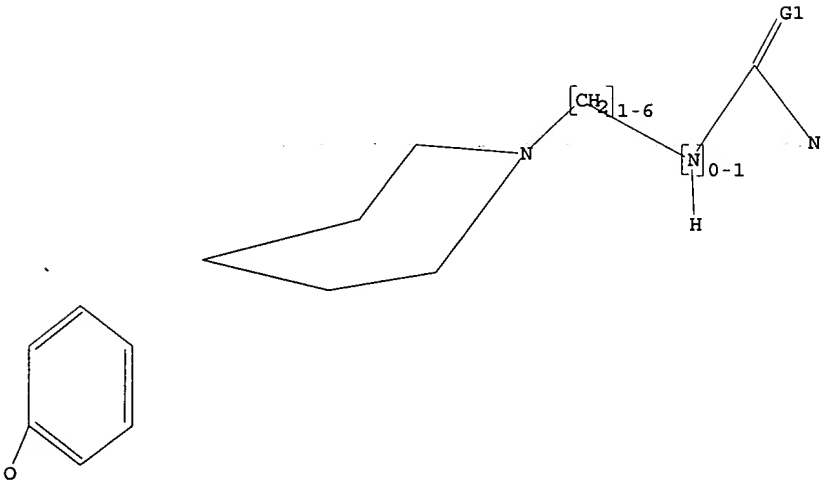
FILE 'STNGUIDE' ENTERED AT 18:49:49 ON 06 AUG 2002

FILE 'REGISTRY' ENTERED AT 18:53:18 ON 06 AUG 2002
L6 STRUCTURE UPLOADED
L7 13 S L6

FILE 'STNGUIDE' ENTERED AT 18:55:02 ON 06 AUG 2002

FILE 'REGISTRY' ENTERED AT 18:57:35 ON 06 AUG 2002
L8 STRUCTURE UPLOADED
L9 0 S L8
L10 0 S L8 SSS FULL

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 O,S,N

Structure attributes must be viewed using STN Express query preparation.

=> d l6
L6 HAS NO ANSWERS
L6 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

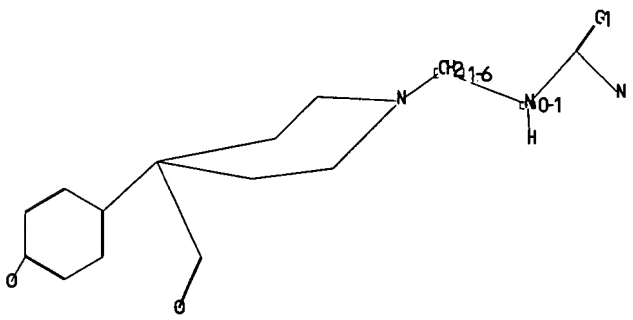
Structure attributes must be viewed using STN Express query preparation.

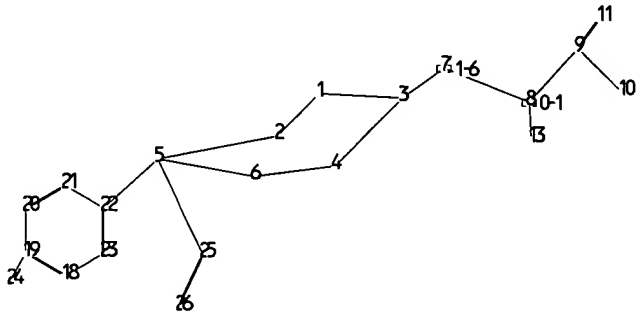
=> d l8
L8 HAS NO ANSWERS
L8 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

C:\STNEXP4\QUERIES\09582059a.str



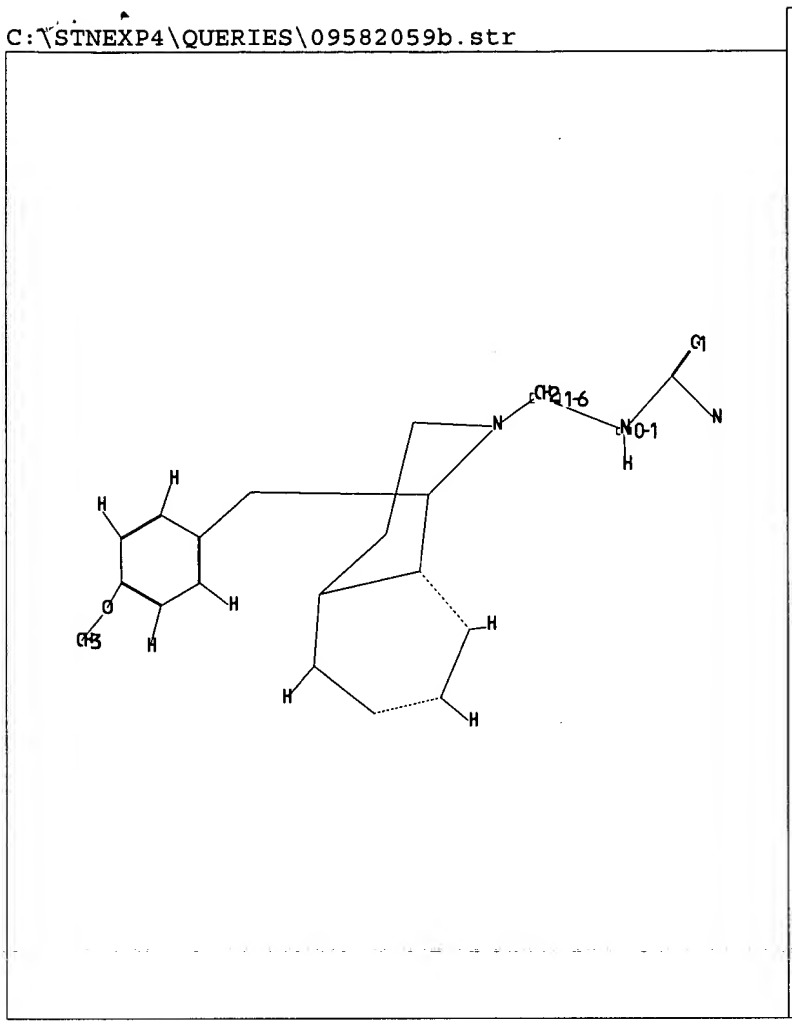


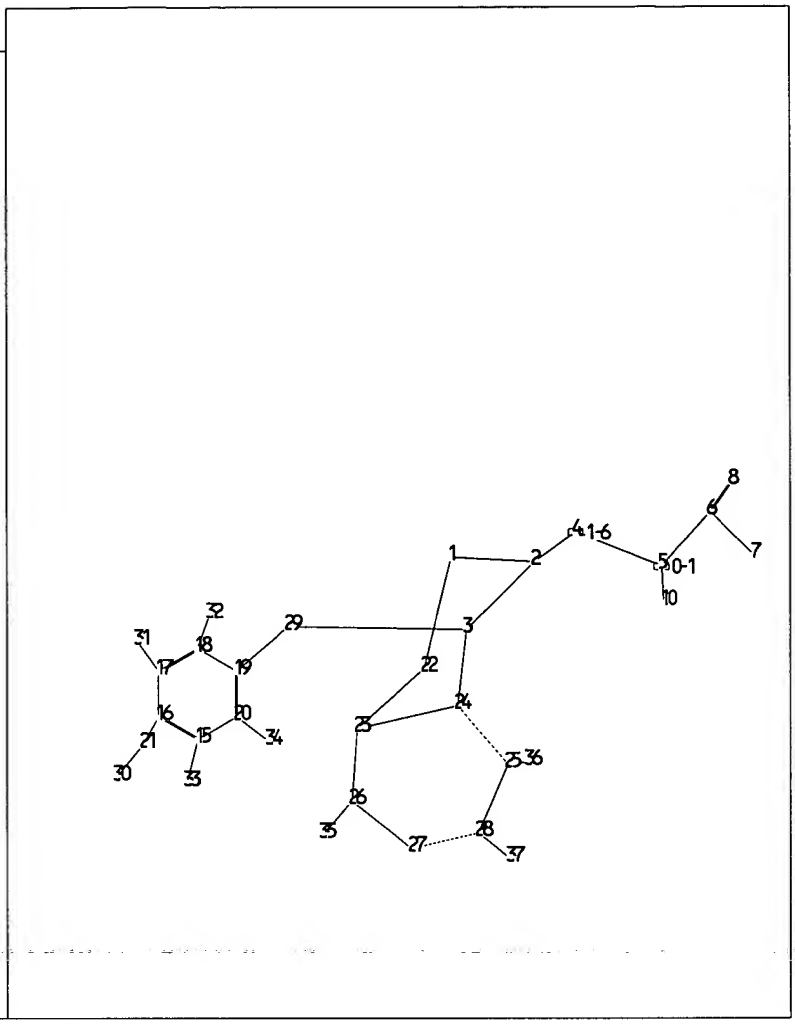
chain nodes :
7 8 9 10 11 13 24 25 26
ring nodes :
1 2 3 4 5 6 18 19 20 21 22 23
chain bonds :
3-7 5-22 5-25 7-8 8-9 8-13 9-10 9-11 19-24 25-26
ring bonds :
1-2 1-3 2-5 3-4 4-6 5-6 18-19 18-23 19-20 20-21 21-22 22-23
exact/norm bonds :
1-2 1-3 2-5 3-4 4-6 5-6 8-9 9-10 9-11 19-24 25-26
exact bonds :
3-7 5-22 5-25 7-8 8-13
normalized bonds :
18-19 18-23 19-20 20-21 21-22 22-23

G1:O,S,N

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 13:CLASS 18:Atom 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:CLASS
25:CLASS 26:CLASS

C:\STNEXP4\QUERIES\09582059b.str





chain nodes :
4 5 6 7 8 10 21 29 30 31 32 33 34 35 36 37
ring nodes :
1 2 3 15 16 17 18 19 20 22 23 24 25 26 27 28
chain bonds :
2-4 3-29 4-5 5-6 5-10 6-7 6-8 15-33 16-21 17-31 18-32 19-29 20-34 21-30 25-36
26-35 28-37
ring bonds :
1-2 1-22 2-3 3-24 15-16 15-20 16-17 17-18 18-19 19-20 22-23 23-24 23-26 24-25
25-28 26-27 27-28
exact/norm bonds :
1-2 1-22 2-3 3-24 5-6 6-7 6-8 16-21 22-23 23-24 23-26 24-25 25-28 26-27 27-28
exact bonds :
2-4 3-29 4-5 5-10 15-33 17-31 18-32 19-29 20-34 21-30 25-36 26-35 28-37
normalized bonds :
15-16 15-20 16-17 17-18 18-19 19-20

G1:O,S,N

Match level :
1:Atom 2:Atom 3:Atom 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 10:CLASS 15:Atom
16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:CLASS 22:Atom 23:Atom 24:Atom 25:Atom
26:Atom 27:Atom 28:Atom 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS
35:CLASS 36:CLASS 37:CLASS

(FILE 'HOME' ENTERED AT 17:41:07 ON 30 JAN 2001)

FILE 'REGISTRY' ENTERED AT 17:41:14 ON 30 JAN 2001
E 142740-96-3/RN
L1 2 S E3-E4
L2 STRUCTURE UPLOADED
L3 0 S L2
L4 104 S L2 SSS FULL

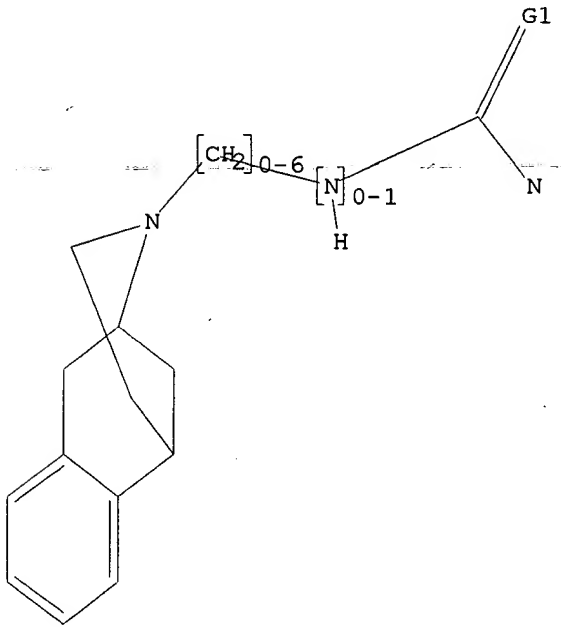
FILE 'CAPLUS' ENTERED AT 18:05:02 ON 30 JAN 2001

=> s l4

L5 37 L4

=> d l2

L2 HAS NO ANSWERS
L2 STR



G1 O,S,N

Structure attributes must be viewed using STN Express query preparation.

=> d 1-37 fbib abs hitstr

L5 ANSWER 1 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 2000:205481 CAPLUS
DN 133:26471
TI Binding of Norbinaltorphimine (norBNI) Congeners to Wild-Type and Mutant

Mu and Kappa Opioid Receptors: Molecular Recognition Loci for the Pharmacophore and Address Components of Kappa Antagonists

AU Larson, Dennis L.; Jones, Robert M.; Hjorth, Siv A.; Schwartz, Thue W.; Portoghese, Philip S.

CS Department of Medicinal Chemistry College of Pharmacy, University of Minnesota, Minneapolis, MN, 55455, USA

SO J. Med. Chem. (2000), 43(8), 1573-1576
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

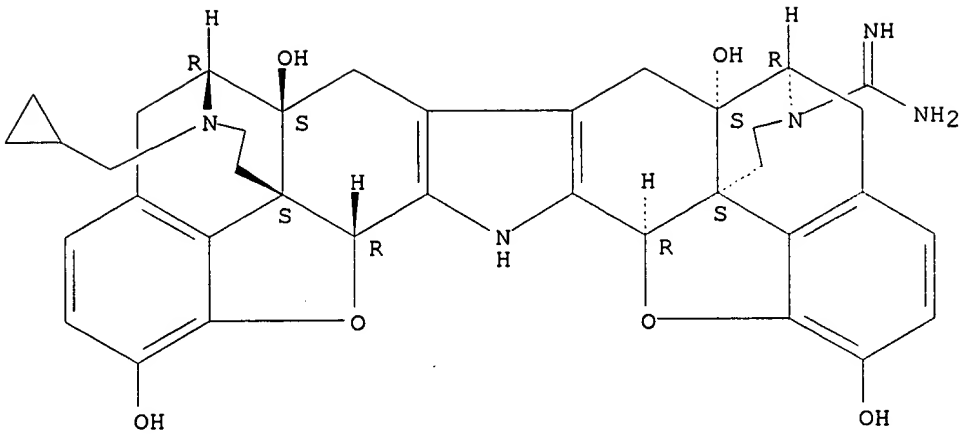
AB Mol. modifications of both the kappa opioid antagonist norbinaltorphimine (norBNI) and the kappa receptor have provided evidence that the selectivity of this ligand is conferred through ionic interaction if its N17' protonated amine group (an "address") with a nonconserved acidic residue (Glu297) on the kappa receptor. In the present study, we have examd. the effect of structural modifications on the affinity of norBNI analogs for wild-type and mutant kappa and mu opioid receptors expressed in COS-7 cells. Compds. which have an antagonist pharmacophore and basic N17' group in common with norBNI, retained high affinity for the wild-type kappa but exhibited greatly reduced affinity for mutant kappa receptors (E297K and E297A). Modification of the phenolic or N-substituent groups of the antagonist pharmacophore or removal of basicity at the address N17' center led to greatly reduced affinity for the wild-type and mutant receptors. The reduced affinity upon modification of the kappa receptor is consistent with the ionic interaction of the protonated N17' group of kappa antagonists with the carboxylate group of E297 at the top of TM6. This was supported by the greatly enhanced affinity of compds. for the mutant mu receptor (K303E), as compared to the wild-type mu receptor, given that residue K303 occupies a position equiv. to that of E297 in the kappa receptor. In view of the high degree of homol. of the seven TM domains of the kappa and mu opioid receptors, it is suggested that the antagonist pharmacophore is bound within this highly conserved region of the kappa or mutant mu receptor and that an anionic residue at the top of TM6 (E297 or K303E, resp.) provides addnl. binding affinity.

IT **273396-05-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and mol. recognition of norbinaltorphimine analogs by wild-type and mutant .mu. and .kappa. opioid receptors)

RN 273396-05-7 CAPLUS

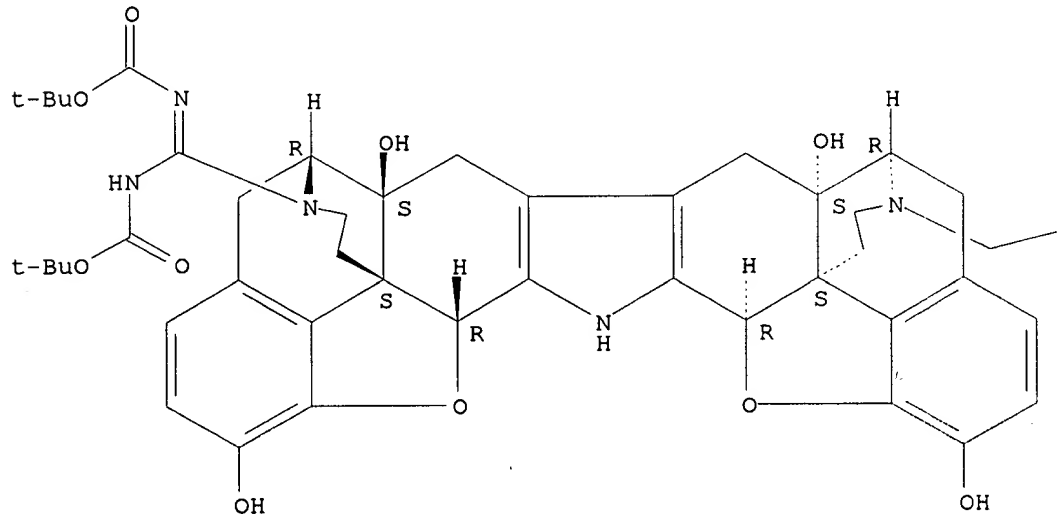
CN 4,8:11,15-Dimethano-20H-bisbenzofuro[2,3-a:3',2'-i]dipyrido[4,3-b:3',4'-h]carbazole-7(8H)-carboximidamide, 12-(cyclopropylmethyl)-5,6,9,7,8a,10,10a,11,12,13,14,19a,20b-dodecahydro-1,8a,10a,18-tetrahydroxy-, (4bS,8R,8aS,10aS,11R,14aS,19aR,20bR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **273396-06-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and mol. recognition of norbinaltorphimine analogs by wild-type
and mutant .mu. and .kappa. opioid receptors)
RN 273396-06-8 CAPLUS
CN Carbamic acid, [[(4bS,8R,8aS,10aS,11R,14aS,19aR,20bR)-12-(cyclopropylmethyl)-5,6,8a,9,10,10a,11,12,13,14,19a,20b-dodecahydro-1,8a,10a,18-tetrahydroxy-4,8:11,15-dimethano-20H-bisbenzofuro[2,3-a:3',2'-i]dipyrido[4,3-b:3',4'-h]carbazol-7(8H)-yl][[(1,1-dimethylethoxy)carbonyl]amino]methylene]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 15
RE
(2) Archer, S; J Med Chem 1985, V28, P974 CAPLUS
(3) Bolognesi, M; J Med Chem 1996, V39, P1816 CAPLUS
(4) Hjorth, S; Mol Pharmacol 1995, V47, P1089 CAPLUS
(5) Jones, R; J Med Chem 1998, V41, P4911 CAPLUS
(6) Kim, K; Tetrahedron Lett 1988, V29, P3183 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1999:495297 CAPLUS
DN 131:144745
TI synthesis and analgesic activity of morphine related compounds
IN Jackson, Roy William; Subasinghe, Kamani Rupika; Boura, Alan Louis Arthur
PA Monash University, Australia; Polychip Pharmaceuticals Pty. Ltd.
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA English

this appl'n

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9938869	A1	19990805	WO 1999-AU62	19990129
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
			AU 1998-1530	19980129
			AU 1998-3114	19980421
			AU 1998-5046	19980804
AU 9924037	A1	19990816	AU 1999-24037	19990129
			AU 1998-1530	19980129
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			AU 1998-5046	19980804
			WO 1999-AU62	19990129
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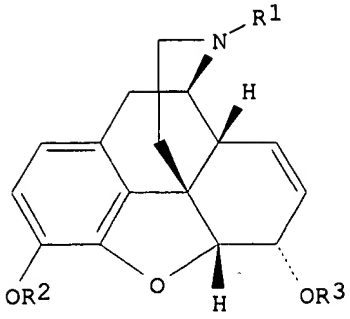
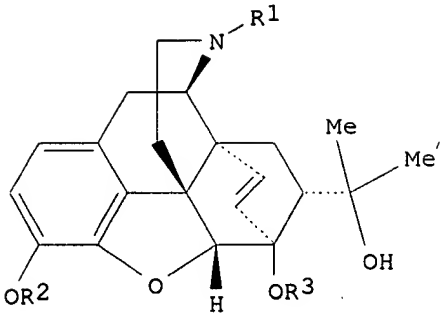
			WO 1999-AU62	19990129

OS MARPAT 131:144745
GI



I



II

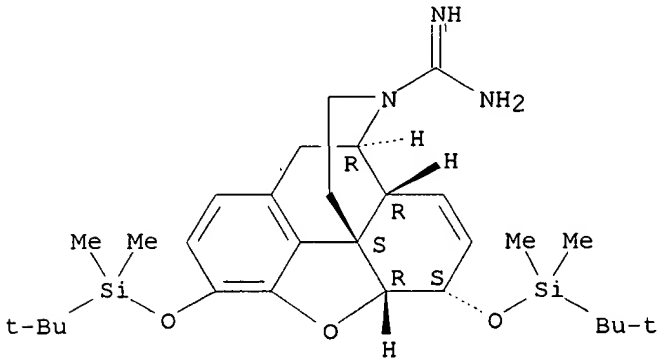
AB Synthesis of opioid compds., particularly morphine (I) [R2, R3 = H, Me; R1
= (CH2)nC(=NH)NH2, n = 0,2,3] and related compds. (II) (etheno or ethano),
or a pharmaceutically acceptable salt (compns. given) is presented. Thus,
II (ethano, n = 3, R2 = H, R3 = Me) (III) was prepd. in 5 steps from 7.alpha.-(1-hydroxy-1-methylethyl)-6,14-endo-ethanotetrahydronororipavine by cyanoethylation, silylation, redn. to Pr amine, aminoimination and desilylation. III was tested for analgesic activity in two mouse models and showed activity at 3 times the morphine concn.

IT **235752-00-8P 235752-03-1P**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant);
SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and analgesic activity of morphine related compds.)

RN 235752-00-8 CAPLUS

CN Morphinan-17-carboximidamide, 7,8-didehydro-3,6-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,5-epoxy-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

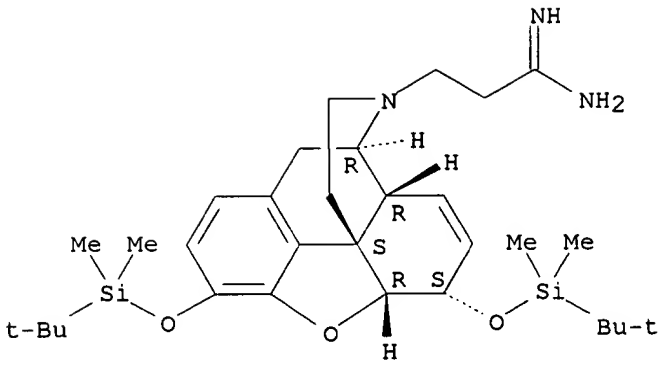
Absolute stereochemistry.



RN 235752-03-1 CAPLUS

CN Morphinan-17-propanimidamide, 7,8-didehydro-3,6-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,5-epoxy-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

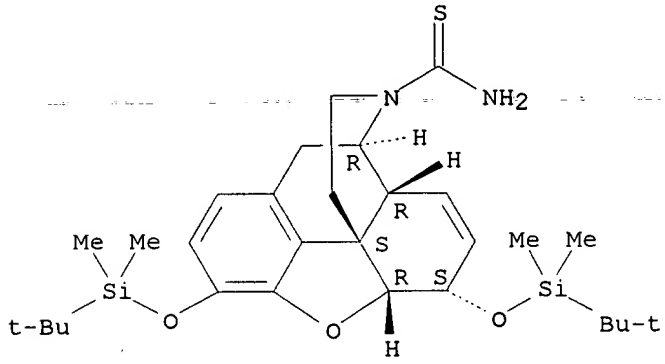


IT **235751-99-2P 235752-01-9P 235752-04-2P**
235752-05-3P 235752-06-4P 235752-07-5P
235752-08-6P 235752-09-7P 235752-10-0P
235752-11-1P 235752-13-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and analgesic activity of morphine related compds.)

RN 235751-99-2 CAPLUS

CN Morphinan-17-carbothioamide, 7,8-didehydro-3,6-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,5-epoxy-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

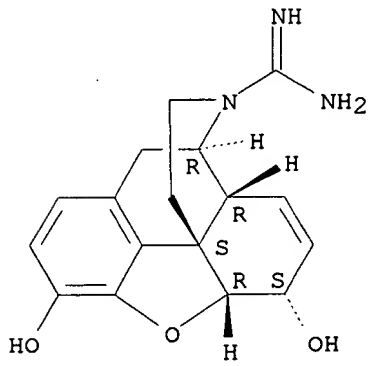
Absolute stereochemistry.



RN 235752-01-9 CAPLUS

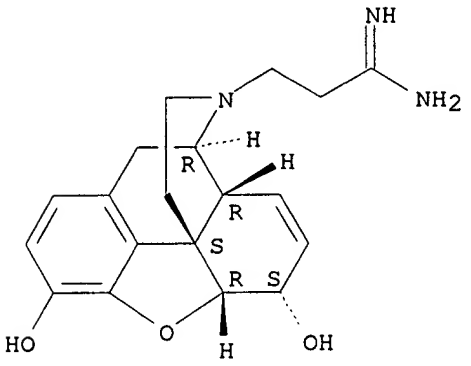
CN Morphinan-17-carboximidamide, 7,8-didehydro-4,5-epoxy-3,6-dihydroxy-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



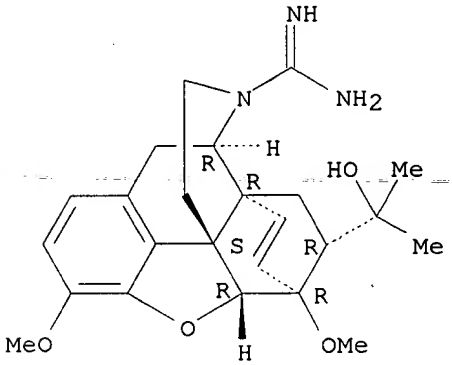
RN 235752-04-2 CAPLUS
CN Morphinan-17-propanimidamide, 7,8-didehydro-4,5-epoxy-3,6-dihydroxy-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



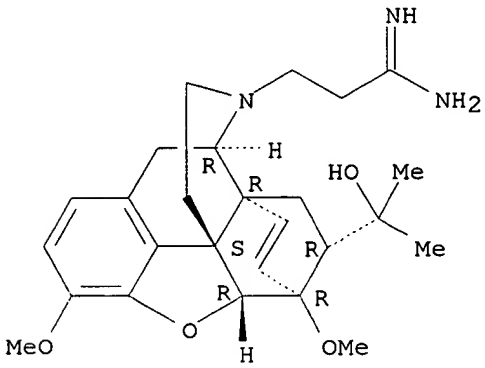
RN 235752-05-3 CAPLUS
CN 6,14-Ethenomorphinan-17-carboxamidamide, 4,5-epoxy-7-(1-hydroxy-1-methylethyl)-3,6-dimethoxy-, (5.alpha.,7.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 235752-06-4 CAPLUS
CN 6,14-Ethenomorphinan-17-propanimidamide, 4,5-epoxy-7-(1-hydroxy-1-methylethyl)-3,6-dimethoxy-, (5.alpha.,7.alpha.)- (9CI) (CA INDEX NAME)

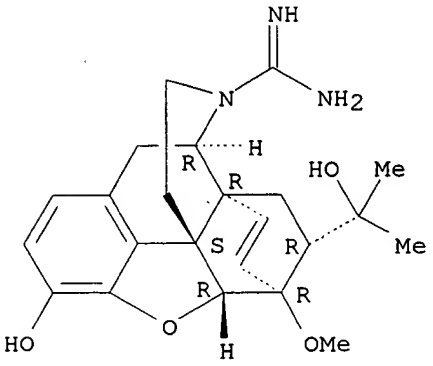
Absolute stereochemistry.



RN 235752-07-5 CAPLUS
CN 6,14-Ethenomorphinan-17-carboxamidamide, 4,5-epoxy-3-hydroxy-7-(1-hydroxy-

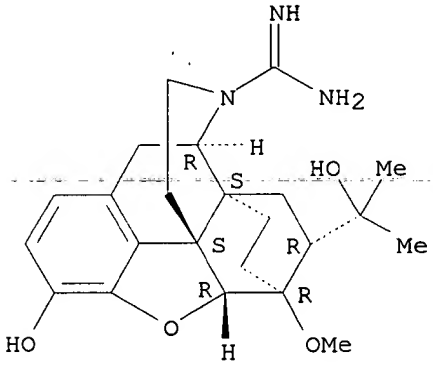
1-methylethyl)-6-methoxy-, (5.alpha.,7.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



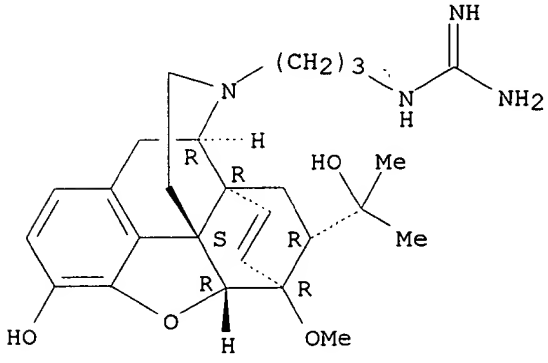
RN 235752-08-6 CAPLUS
CN 6,14-Ethenomorphinan-17-carboximidamide, 4,5-epoxy-18,19-dihydro-3-hydroxy-7-(1-hydroxy-1-methylethyl)-6-methoxy-, (5.alpha.,7.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 235752-09-7 CAPLUS
CN Guanidine, [3-[(5.alpha.,7.alpha.)-4,5-epoxy-3-hydroxy-7-(1-hydroxy-1-methylethyl)-6-methoxy-6,14-ethenomorphinan-17-yl]propyl]- (9CI) (CA INDEX NAME)

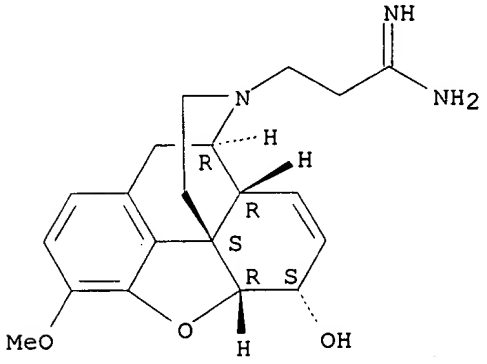
Absolute stereochemistry.



RN 235752-10-0 CAPLUS

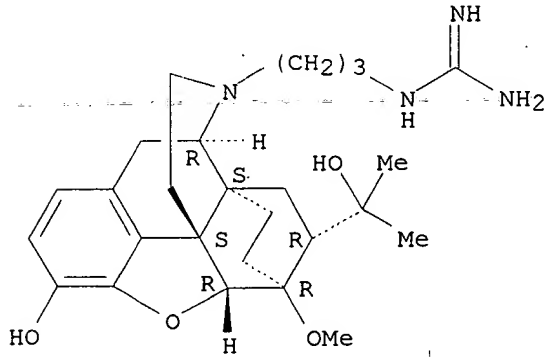
CN Morphinan-17-propanimidamide,
7,8-didehydro-4,5-epoxy-6-hydroxy-3-methoxy-
, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



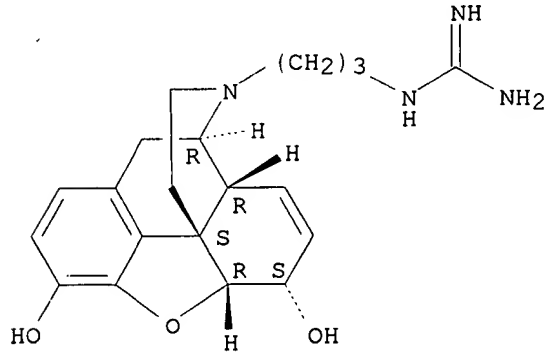
RN 235752-11-1 CAPLUS
CN Guanidine,
[3-[(5.alpha.,7.alpha.)-4,5-epoxy-18,19-dihydro-3-hydroxy-7-(1-
hydroxy-1-methylethyl)-6-methoxy-6,14-ethenomorphinan-17-yl]propyl]-
(9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 235752-13-3 CAPLUS
CN Morphinan-3,6-diol, 17-[3-[(aminoiminomethyl)amino]propyl]-7,8-didehydro-
4,5-epoxy-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

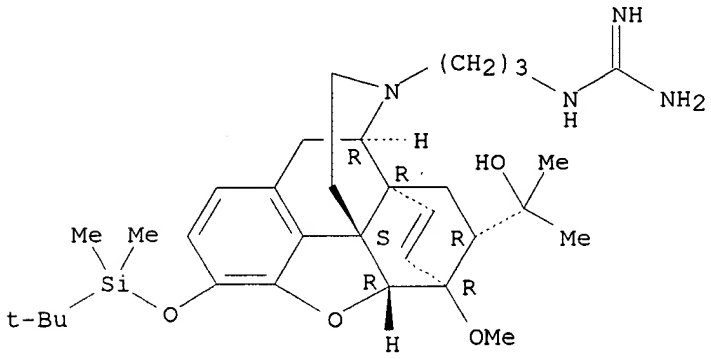
Absolute stereochemistry.



IT **235752-25-7P 235752-27-9P 235752-31-5P**
235752-34-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(synthesis and analgesic activity of morphine related compds.)

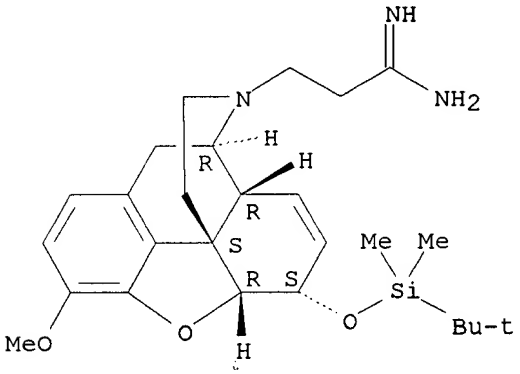
RN 235752-25-7 CAPLUS
CN Guanidine,
[3-[(5.alpha.,7.alpha.)-3-[[(1,1-dimethylethyl)dimethylsilyl]ox
y]-4,5-epoxy-7-(1-hydroxy-1-methylethyl)-6-methoxy-6,14-ethenomorphinan-17-yl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



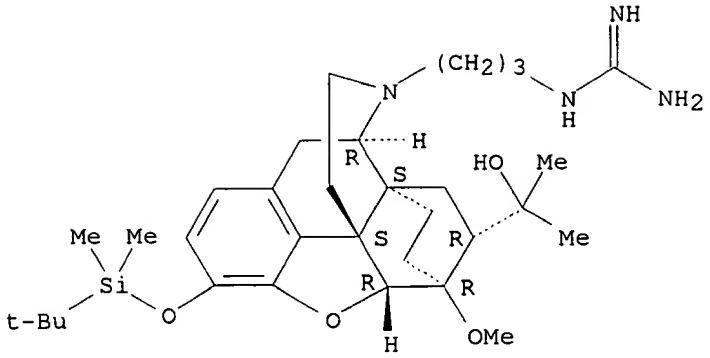
RN 235752-27-9 CAPLUS
CN Morphinan-17-propanimidamide, 7,8-didehydro-6-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,5-epoxy-3-methoxy-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



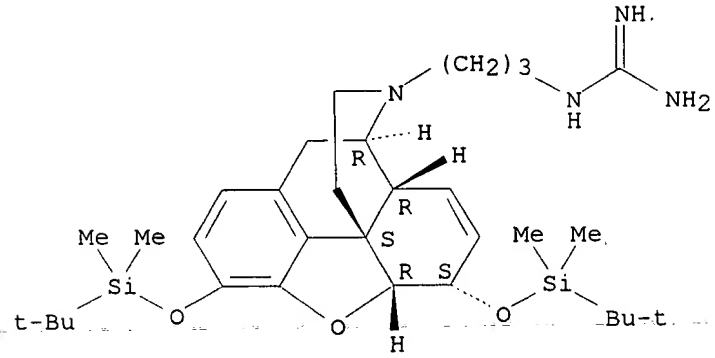
RN 235752-31-5 CAPLUS
CN Guanidine,
[3-[(5.alpha.,7.alpha.)-3-[[(1,1-dimethylethyl)dimethylsilyl]ox
y]-4,5-epoxy-18,19-dihydro-7-(1-hydroxy-1-methylethyl)-6-methoxy-6,14-ethenomorphinan-17-yl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 235752-34-8 CAPLUS
CN Guanidine, [3-[(5.alpha.,6.alpha.)-7,8-didehydro-3,6-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,5-epoxymorphinan-17-yl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 2
RE
(1) Anon; Clin Exp Pharmacol Physiol 1992, V19(11), P17 CAPLUS
(2) Portoghese, P; US 4806556 1989 CAPLUS

L5 ANSWER 3 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1999:405112 CAPLUS
DN 131:56155
TI Methods for the simultaneous identification of novel biological targets and lead structures for drug development using combinatorial libraries and probes
IN Heefner, Donald L.; Zepp, Charles M.; Gao, Yun; Jones, Steven W.
PA Sepracor Inc., USA
SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9931267	A1	19990624	WO 1998-US26894	19981218

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

			US 1997-68035	19971218
AU 9919256	A1	19990705	AU 1999-19256	19981218
			US 1997-68035	19971218
			WO 1998-US26894	19981218
EP 1049796	A1	20001108	EP 1998-964053	19981218

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

US 1997-68035	19971218	
WO 1998-US26894	19981218	

PATENT FAMILY INFORMATION:

FAN 1999:405125

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9931280	A1	19990624	WO 1998-US26945	19981218

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

			US 1997-68035	19971218
AU 9919278	A1	19990705	AU 1999-19278	19981218
			US 1997-68035	19971218
			WO 1998-US26945	19981218
EP 1038037	A1	20000927	EP 1998-964080	19981218

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

US 1997-68035	19971218	
WO 1998-US26945	19981218	

AB The combinatorial screening assays and detection methods of the present invention encompass highly diversified libraries of compds. which act as fingerprints to allow for the identification of specific mol. differences existing between biol. samples. The combinatorial screening assay and detection methods of the present invention utilize highly diversified libraries of compds. to interrogate and characterize complex mixts. in order to identify specific mol. differences existing between biol. samples, which may serve as targets for diagnosis of development of therapeutics. The invention is base, in part, on the design of sensitive, rapid, homogeneous assay systems that permit the evaluation, interrogation, and characterization of samples using complex, highly diversified libraries of mol. probes. The ability to run the high throughput assays in a homogeneous format increases sensitivity of screening. In addn., the homogeneous format allows the mols. which interact to maintain their native or active conformations. Moreover, the homogeneous assay systems of the invention utilize robust detection systems that do not require sepn. steps for detection of reaction products. The assays of the invention can be used for diagnostics, drug screening and discovery, target-driven discover, and in the field of proteomics and genomics for the identification of disease markers and drug targets.

IT **228112-27-4**

RL: ARU (Analytical role, unclassified); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)

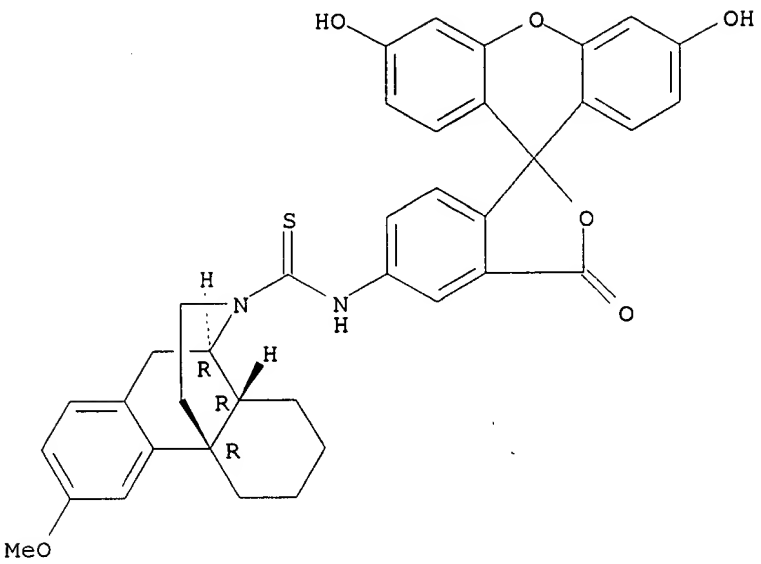
(identification of novel biol. targets and lead structures for drug development using combinatorial libraries and probes)

RN 228112-27-4 CAPLUS

CN Morphinan-17-carbothioamide, N-(3',6'-dihydroxy-3-oxospiro[isobenzofuran-

1(3H),9'-[9H]xanthen]-5-yl)-3-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

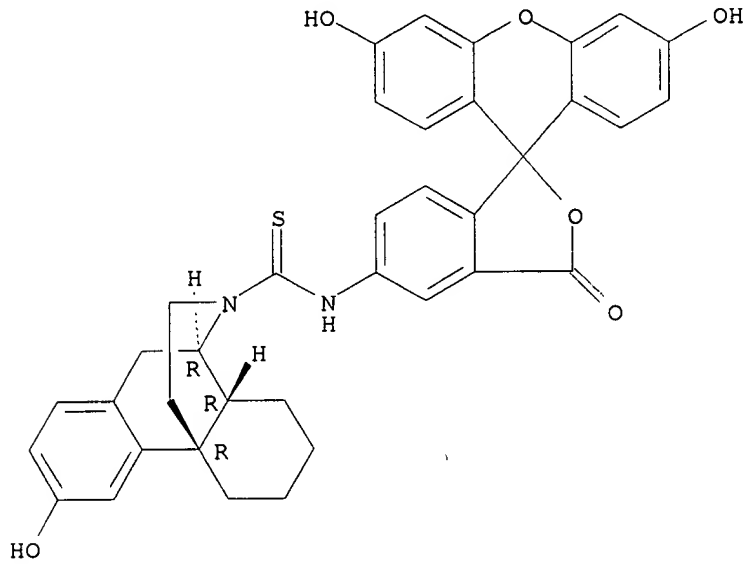


IT **228112-11-6P 228112-23-0P 228112-24-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(ligand; identification of novel biol. targets and lead structures for drug development using combinatorial libraries and probes)

RN 228112-11-6 CAPLUS

CN Morphinan-17-carbothioamide, N-(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)-3-hydroxy- (9CI) (CA INDEX NAME)

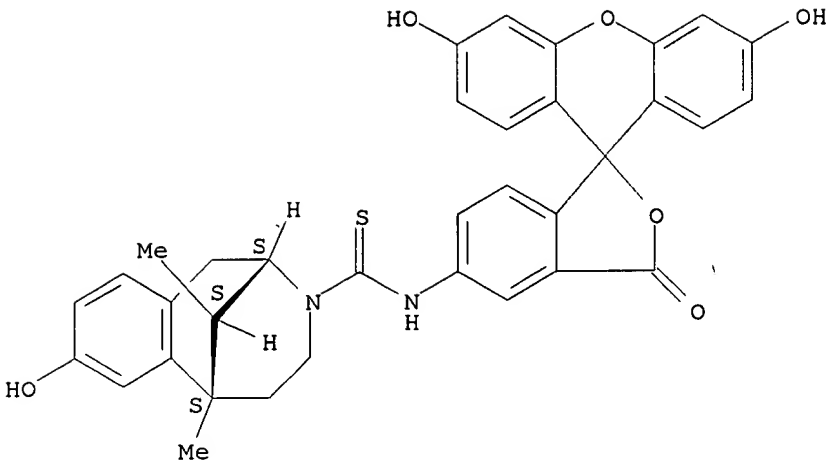
Absolute stereochemistry.



RN 228112-23-0 CAPLUS

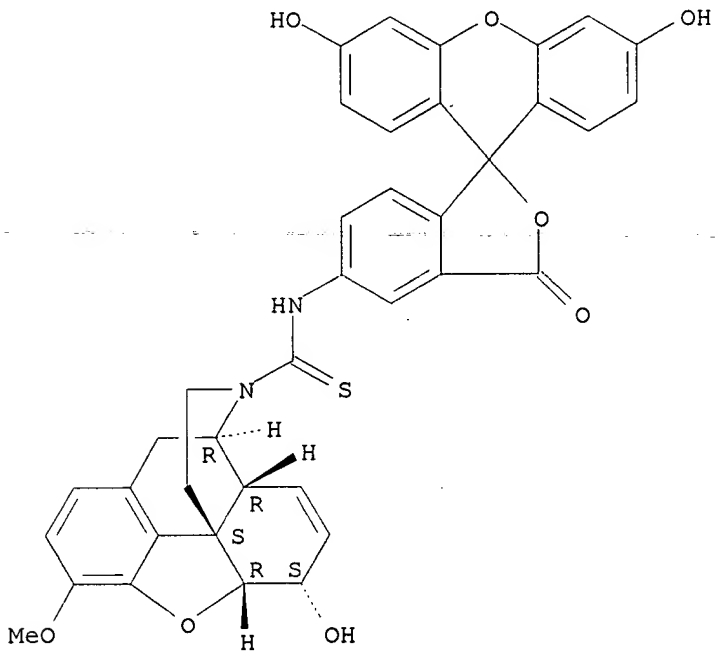
CN 2,6-Methano-3-benzazocine-3(2H)-carbothioamide, N-(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)-1,4,5,6-tetrahydro-8-hydroxy-6,11-dimethyl-, (2S,6S,11S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 228112-24-1 CAPLUS
CN Morphinan-17-carbothioamide, N-(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)-4,5-epoxy-6-hydroxy-3-methoxy-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 1
RE
(1) Lin; Science 1997, V278, P840 CAPLUS

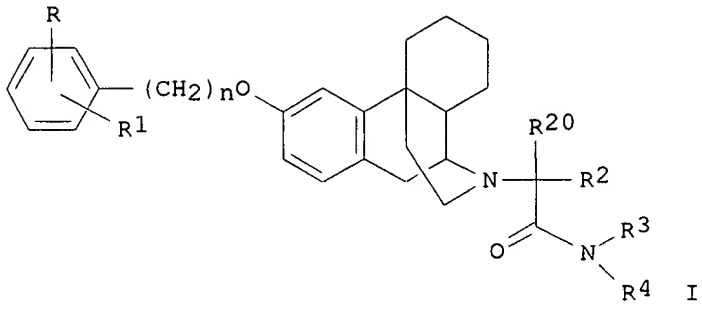
L5 ANSWER 4 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1998:682234 CAPLUS
DN 129:290270
TI Preparation of aralkoxymorphinan derivatives for treatment of central nervous system disorders
IN Varasi, Mario; Pevarello, Paolo; Traquandi, Gabriella; Amici, Raffaella; Salvati, Patricia
PA Pharmacia and Upjohn S.p.A., Italy
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 1

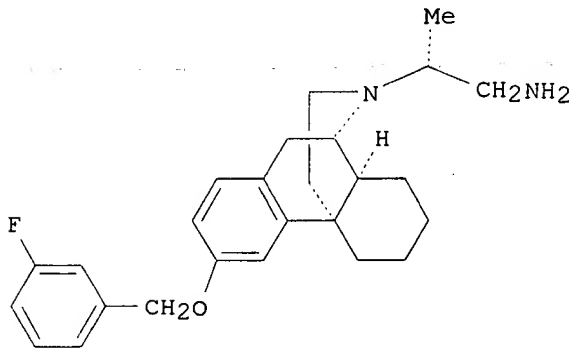
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9843961	A1	19981008	WO 1998-EP1927	19980327
W: AL, AU, BG, BR, CA, CN, CZ, EE, HU, IL, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
			GB 1997-6753	19970403
AU 9875215	A1	19981022	AU 1998-75215	19980327
			GB 1997-6753	19970403
			WO 1998-EP1927	19980327

OS MARPAT 129:290270
GI

not prior art



I



II

AB Novel 1,3,4,9,10,10a-hexahydro-6-substituted-11-(14-alkylacetamido)-2H-10,4a-(iminoethano)phenanthrene derivs., I (n = 0, 1, 2 or 3; R and R1 being the same or different is H, halo, hydroxy, trifluoromethyl, cyano, nitro, Ph, benzyl, C1-C6 alkyl, C1-C6 alkoxy, C1-C6 alkylthio, SOR5, SO2R5, SO2NH2, formyl, C2-C6 alkanoyl, carboxy, C1-C6 alkoxy-carbonyl or -NR6R7 in which R6 and R7 independently is H, C1-C6 alkyl, formyl, or C2-C6 alkanoyl and R5 is hydrogen or C1-C6 alkyl; R2 and R20, being the same or different, is hydrogen, C1-C6 alkyl unsubstituted or substituted by hydroxy or by a Ph ring in its turn optionally substituted by 1 to 4 substituents independently chosen from halogen, C1-C6 alkyl, C1-C6 alkoxy and trifluoromethyl; or R2 and R20 taken together with the adjacent carbon atom form a C3-C6 cycloalkyl ring; R3 and R4, which are the same or different, is hydrogen or C1-C6 alkyl) and the pharmaceutically acceptable salts were prepd. as agents active on the central nervous system. Thus, 4a(S),10(S),10a(S)-1,3,4,9,10,10a-hexahydro-6-hydroxy-2H-10,4a-(iminoethano)phenanthrene-11-carboxylic acid 2,2,2-trichloroethyl ester

was treated with 3-fluorobenzyl chloride followed by removal of the trichloroethoxycarbonyl group and reaction with L-Et lactate and trifluoromethanesulfonic anhydride followed by hydrolysis and amidation with NH3 to give 4a(S),10(S),10a(S),14(R)-1,3,4,9,10,10a-hexahydro-6-(3-fluorobenzyloxy)-11-(14-methylacetamido)-2H-10,4a-(iminoethano)phenanthrene (II). Capsules contg II were prepd.

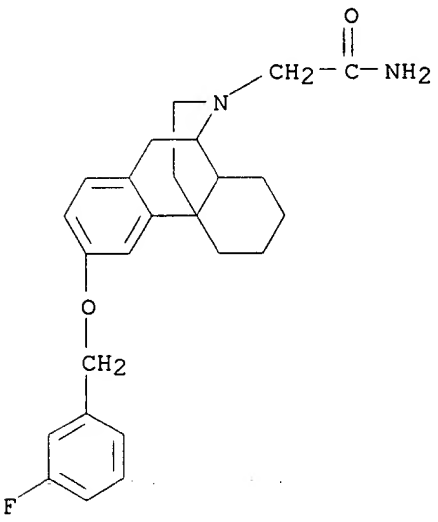
IT **214326-31-5P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of aralkoxymorphinan derivs. for treatment of central nervous system disorders)

RN 214326-31-5 CAPLUS

CN Morphinan-17-acetamide, 3-[(3-fluorophenyl)methoxy]-, (9.xi.,13.xi.,14.xi.)- (9CI) (CA INDEX NAME)



L5 ANSWER 5 OF 37 CAPLUS COPYRIGHT 2001 ACS

AN 1997:549379 CAPLUS

DN 127:162011

TI Preparation of heterocycle-condensed morphinoid derivatives for use as analgesics

IN Dondio, Giulio; Ronzoni, Silvano; Gatti, Pier Andrea; Graziani, Davide

PA Smithkline Beecham S.P.A., Italy; Dondio, Giulio; Ronzoni, Silvano; Gatti, Pier Andrea; Graziani, Davide

SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9725331	A1	19970717	WO 1997-EP120	19970108

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

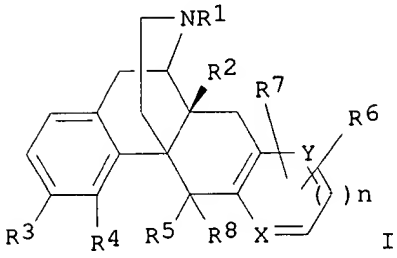
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

	IT 1996-MI29	19960110
	IT 1996-MI2291	19961105

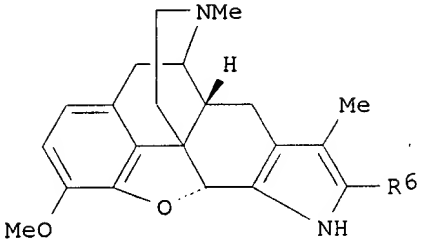
CA 2242609	AA	19970717	CA 1997-2242609	19970108
			IT 1996-MI29	19960110
			IT 1996-MI2291	19961105
AU 9714410	A1	19970801	AU 1997-14410	19970108
AU 706370	B2	19990617		
			IT 1996-MI29	19960110
			IT 1996-MI2291	19961105
			WO 1997-EP120	19970108
EP 880526	A1	19981202	EP 1997-901009	19970108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO				
			IT 1996-MI29	19960110
			IT 1996-MI2291	19961105
			WO 1997-EP120	19970108
CN 1213372	A	19990407	CN 1997-192879	19970108
			IT 1996-MI29	19960110
			IT 1996-MI2291	19961105
BR 9707136	A	19990831	BR 1997-7136	19970108
			IT 1996-MI29	19960110
			IT 1996-MI2291	19961105
			WO 1997-EP120	19970108
JP 2000503019	T2	20000314	JP 1997-524871	19970108
			IT 1996-MI29	19960110
			IT 1996-MI2291	19961105
			WO 1997-EP120	19970108
ZA 9700172	A	19980709	ZA 1997-172	19970109
			IT 1996-MI29	19960110
NO 9803169	A	19980909	NO 1998-3169	19980709
			IT 1996-MI29	19960110
			IT 1996-MI2291	19961105
			WO 1997-EP120	19970108

OS MARPAT 127:162011

GI



I



II

AB Substituted mono heterocycle-condensed morphinoid derivs. I [R1 = H, alkyl, cycloalkyl, alkenyl, aryl, aralkyl; R2 = H, OH, alkoxy, halogen, NO2, amino, SH; R3 = H, alkyl, OH, alkoxy, halogen; R4 = R5 = H, OH, alkoxy, OPh; or R4R5 = O; R6 = carboxamide, acyl, thioacyl, carboxyl; R7 = H, alkyl, alkenyl, halogen; R8 = H, alkyl; X = Y = CH, O, S, NR1; n = 0, 1], potent and selective delta opioid agonists and antagonists, were prepd for use as analgesics and for treating pathol. conditions which, customarily, can be treated with agonists and antagonists of the delta opioid receptor. Thus, morphinoid II [R6 = CON(CHMe2)CH2Ph] was prepd. by cyclization of 7,8-dihydrocodeinone and N-benzyl-N-isopropyl-2-phenylhydrazone. The morphinoid compds. showed affinities for the delta receptor ranging from 0.5 to 200 nM with delta selectivity ranging from

20

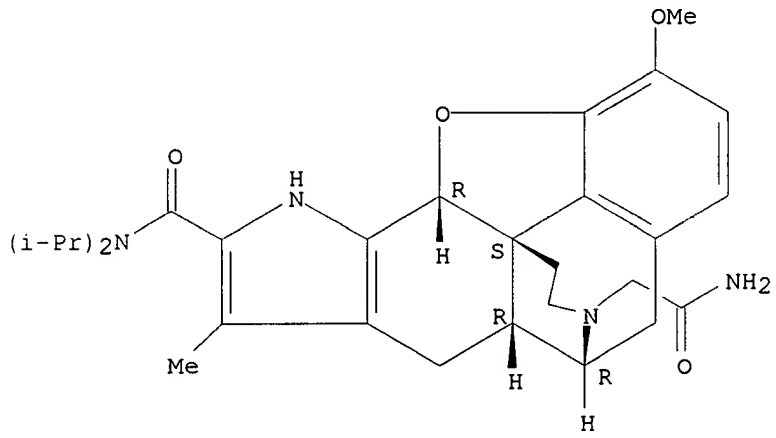
- 1500 times with respect to other opioid receptor types.

IT **193613-24-0P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocycle-condensed morphinoid derivs., potent and selective delta opioid agonists and antagonists, for analgesic and other pharmacol. uses)

RN 193613-24-0 CAPLUS

CN 4,8-Methanobenzofuro[3,2-e]pyrrolo[2,3-g]isoquinoline-7(8H)-acetamide, 11-[[bis(1-methylethyl)amino]carbonyl]-5,6,8a,9,12,12b-hexahydro-1-methoxy-10-methyl-, [8R-(4bS*,8.alpha.,8a.beta.,12b.beta.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L5 ANSWER 6 OF 37 CAPLUS COPYRIGHT 2001 ACS

AN 1995:969421 CAPLUS

DN 124:7968

TI Modular design and synthesis of aminimide-containing molecules

IN Hogan, Joseph C., Jr.; Casebier, David; Furth, Paul; Tu, Cheng

PA Arqule Partners, L.P., USA

SO PCT Int. Appl., 208 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9518186	A1	19950706	WO 1993-US12612	19931228
	W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, UZ				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2179983	AA	19950706	CA 1993-2179983	19931228
				WO 1993-US12612	19931228
	AU 9460159	A1	19950717	AU 1994-60159	19931228
	AU 689764	B2	19980409		
				WO 1993-US12612	19931228
	EP 737232	A1	19961016	EP 1994-906465	19931228
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
				WO 1993-US12612	19931228
	JP 09510693	T2	19971028	JP 1993-517995	19931228
				WO 1993-US12612	19931228
	CN 1105355	A	19950719	CN 1993-121725	19931230

OS CASREACT 124:7968
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

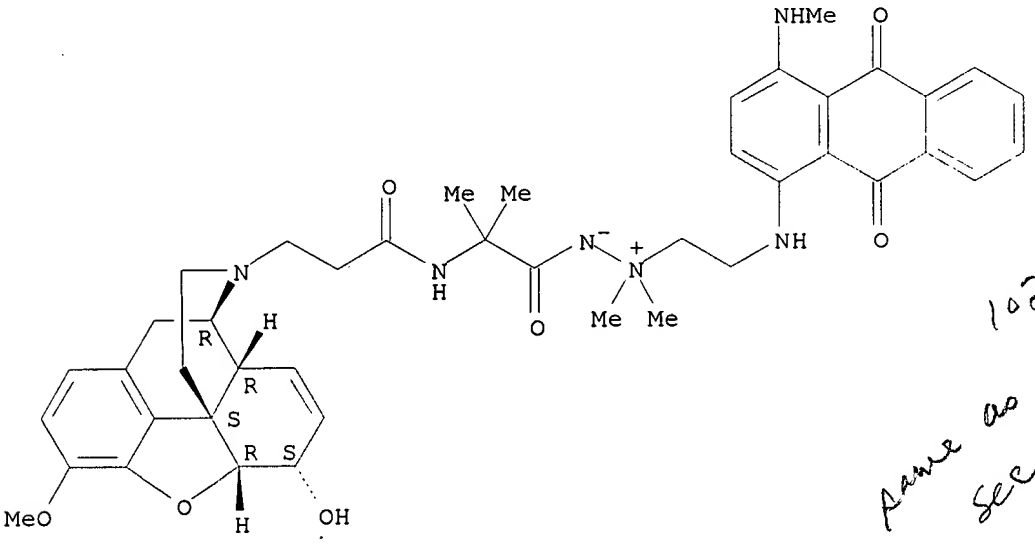
AB The design and synthesis of a variety of aminimide-derived mol. modules and their use in the construction of new mols. and fabricated materials is disclosed. The new mols. and fabricated materials are mol. recognition agents useful in the design and synthesis of drugs, and have applications in sepns. and materials science. Examples given include monomers/polymers, drug conjugates, mimetics of peptides, (oligo)nucleotides, carbohydrates, and lipids, and a combinatorial library (matrix of 16). For instance, the (uridylmethyl)propylhydrazine I was acylated with acetyl chloride and alkylated with tert-Bu bromoacetate to give the aminimide II, which was deprotected with CF3CO2H. The resulting acid was used to perform a similar acylation of a similarly prepd. (cytidylmethyl)propylhydrazine, followed by another alkylation with tert-Bu bromoacetate. A 3rd cycle using I gave the tris(aminimide) III, which presents the sequence U-C-U as a recognition sequence for the RNA codon A-G-A.

IT **154942-11-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of aminimide-contg. mols.)

RN 154942-11-7 CAPLUS

CN Hydrazinium, 2-[2-[[3-[(5.alpha.,6.alpha.)-7,8-didehydro-4,5-epoxy-6-hydroxy-3-methoxymorphinan-17-yl]-1-oxopropyl]amino]-2-methyl-1-oxopropyl]-1-[2-[[9,10-dihydro-4-(methylamino)-9,10-dioxo-1-anthracenyl]amino]ethyl]-1,1-dimethyl-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



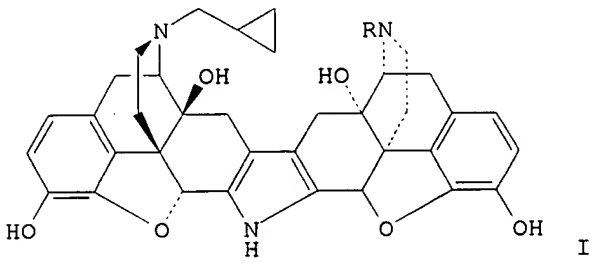
L5 ANSWER 7 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1994:409788 CAPLUS
DN 121:9788
TI Structure-Activity Relationship of N17'-Substituted Norbinaltorphimine

Congeners. Role of the N17' Basic Group in the Interaction with a Putative
Address Subsite on the .kappa. Opioid Receptor

AU Portoghese, P. S.; Lin, C.-E.; Farouz-Grant, F.; Takemori, A. E.
CS College of Pharmacy, University of Minnesota, Minneapolis, MN, 55455, USA

SO J. Med. Chem. (1994), 37(10), 1495-500
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English

GI



I

AB A series of norbinaltorphimine congeners I (R = H, Et, Bu, pentyl, CH2CH2Ph, CH2CH2NHCO2CH2Ph, CH2CH2NH2, CH2CH2NHC(:NH)NH2, Ac, COCH2NH2, COCH2NHCOCH2NH2) have been synthesized in order to evaluate the role of N-17' in conferring .kappa. opioid antagonist selectivity at opioid receptor sites. The compds. that contain a basic N-17' nitrogen are selective .kappa. antagonists. Amidation of N-17' afforded congeners with feeble .kappa. antagonist potency and low selectivity. The fact that potent antagonism and selectivity were obsd. only in I contg. a basic N-17' nitrogen suggests that it interacts with extracellular domains of the .kappa. receptor that contain acidic amino acid residues. The N-terminal domain and extracellular loop 2, both of which contain acidic residues, are candidates for this interaction and may be components of the .kappa. address subsite of the receptor.

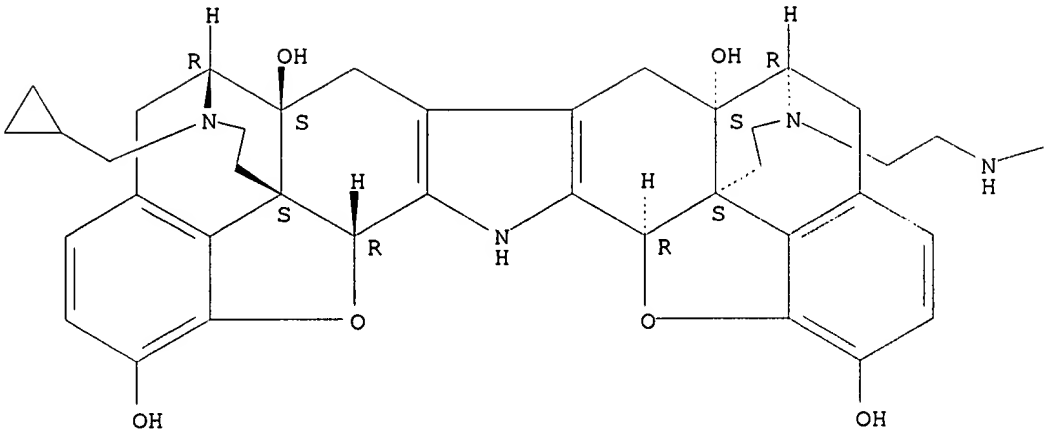
IT **155445-82-2P 155445-83-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and .kappa. opioid receptor binding of)

RN 155445-82-2 CAPLUS

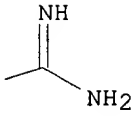
CN Guanidine, [2-[12-(cyclopropylmethyl)-5,6,9,10,11,12,13,14,19a,20b-decahydro-1,8a,10a,18-tetrahydroxy-4,8:11,15-dimethano-20H-bisbenzofuro[2,3-a:3',2'-i]dipyrido[4,3-b:3',4'-h]carbazol-7(8H)-yl]ethyl]-, [8R-(4bS*,8.alpha.,8a.beta.,10a.alpha.,11.beta.,14aS*,19a.alpha.,20b.beta.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



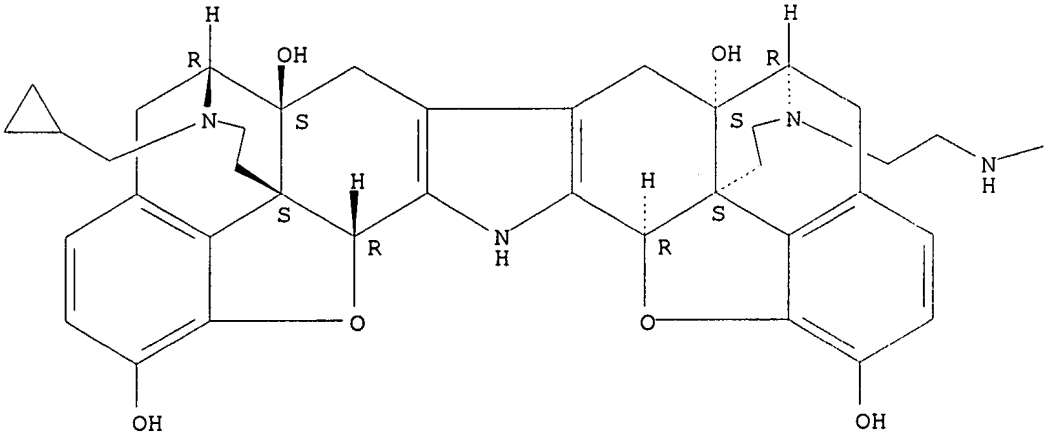
RN 155445-83-3 CAPLUS
CN Guanidine, [2-[12-(cyclopropylmethyl)-5,6,9,10,11,12,13,14,19a,20b-decahydro-1,8a,10a,18-tetrahydroxy-4,8:11,15-dimethano-20H-bisbenzofuro[2,3-a:3',2'-i]dipyrido[4,3-b:3',4'-h]carbazol-7(8H)-yl]ethyl]-, [8R-(4bS*,8.alpha.,8a.beta.,10a.alpha.,11.beta.,14aS*,19a.alpha.,20b.beta.)]-, sulfate (1:1) (salt) (9CI) (CA INDEX NAME)

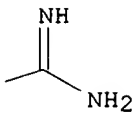
CM 1

CRN 155445-82-2
CMF C39 H44 N6 O6
CDES *

Absolute stereochemistry.

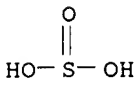
PAGE 1-A





CM 2

CRN 7782-99-2
CMF H2 O3 S



L5 ANSWER 8 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1994:280277 CAPLUS
DN 120:280277
TI Aminimide-containing molecules and materials as molecular recognition agents
IN Hogan, Joseph C., Jr.
PA Legomer Partners, L.P., USA
SO PCT Int. Appl., 128 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9401102	A1	19940120	WO 1993-US6241	19930630
	W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
				US 1992-906769	19920630
				US 1992-906770	19920630
				US 1993-41559	19930402
	AU 9346592	A1	19940131	AU 1993-46592	19930630
	AU 685752	B2	19980129		
				US 1992-906769	19920630
				US 1992-906770	19920630
				US 1993-41559	19930402
				WO 1993-US6241	19930630
	JP 08500339	T2	19960116	JP 1993-503400	19930630
				US 1992-906769	19920630
				US 1992-906770	19920630
				US 1993-41559	19930402
				WO 1993-US6241	19930630
	EP 723441	A1	19960731	EP 1993-916884	19930630
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
				US 1992-906769	19920630
				US 1992-906770	19920630
				US 1993-41559	19930402
				WO 1993-US6241	19930630

BR 9306657	A	19981208	BR 1993-6657	19930630
			US 1992-906769	19920630
			US 1992-906770	19920630
			US 1993-41559	19930402
			WO 1993-US6241	19930630
US 5705585	A	19980106	US 1995-204206	19950327
			WO 1993-US6241	19930630
US 5981467	A	19991109	US 1996-765173	19960216
			US 1995-204206	19950327

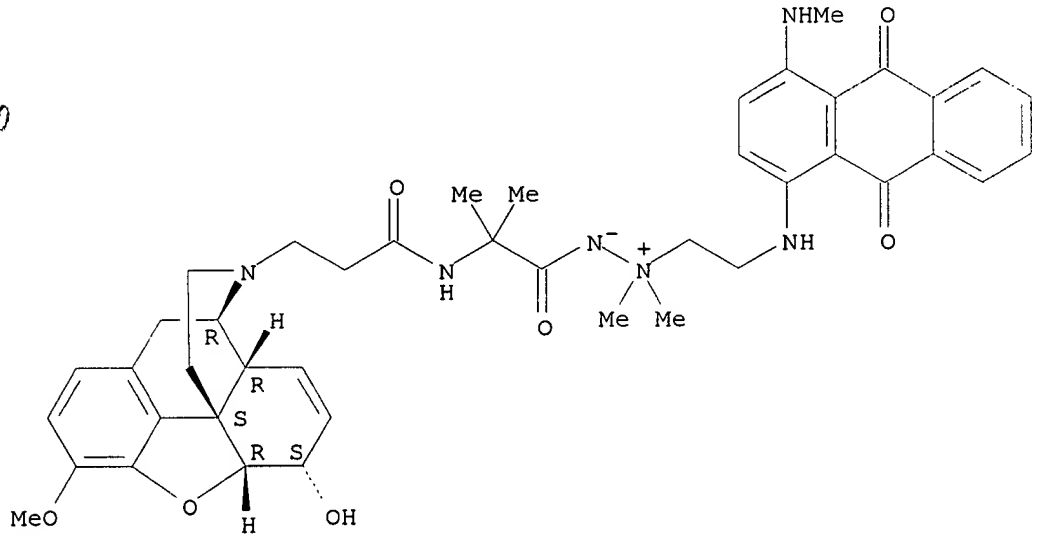
AB The design and synthesis of novel aminimide-based mol. modules and the use of the modules in the construction of new mols. and fabricated materials are disclosed. The new mols. and fabricated materials are mol. recognition agents useful in the design and synthesis of drugs and have applications in sepns. and materials science. For example, 1,2-epoxydodecane is reacted with vincamine and 1,1-dimethylhydrazine to give a conjugate, which is useful as a stabilization agent for the isolation and purifn. of receptor proteins which are therapeutically acted upon by vincamine and by structurally related mols.

IT **154942-11-7P**
RL: PREP (Preparation)
(prepn. of, as probe for isolation of codeine-binding receptor proteins)

RN 154942-11-7 CAPLUS

CN Hydrazinium, 2-[2-[[3-[(5.alpha.,6.alpha.)-7,8-didehydro-4,5-epoxy-6-hydroxy-3-methoxymorphinan-17-yl]-1-oxopropyl]amino]-2-methyl-1-oxopropyl]-1-[2-[[9,10-dihydro-4-(methylamino)-9,10-dioxo-1-anthracenyl]amino]ethyl]-1,1-dimethyl-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

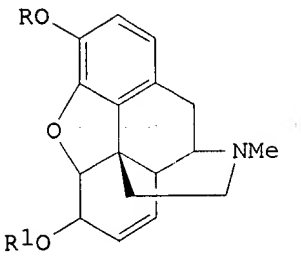


L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1994:134898 CAPLUS
DN 120:134898
TI Preparation of functionalized morphine derivatives as hapten conjugate intermediates
IN Buechler, Kenneth Francis
PA Biosite Diagnostics Incorp., USA
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9320079	A1	19931014	WO 1993-US3009	19930331
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
			US 1992-864107	19920406
AU 9339418	A1	19931108	AU 1993-39418	19930331
			US 1992-864107	19920406
			WO 1993-US3009	19930331
EP 635019	A1	19950125	EP 1993-908688	19930331
EP 635019	B1	19990526		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
			US 1992-864107	19920406
			WO 1993-US3009	19930331
JP 07505634	T2	19950622	JP 1993-517657	19930331
			US 1992-864107	19920406
			WO 1993-US3009	19930331
AT 180484	E	19990615	AT 1993-908688	19930331
			US 1992-864107	19920406
US 5610283	A	19970311	US 1995-389969	19950215
			US 1992-864107	19920406

OS MARPAT 120:134898
GI



I

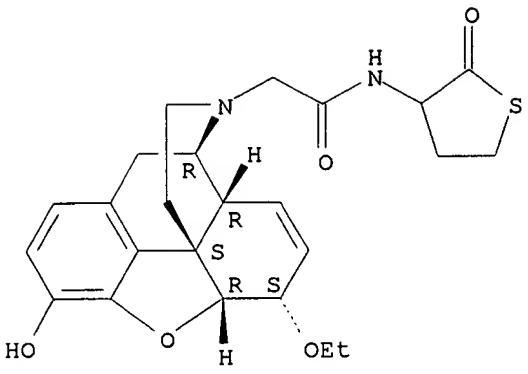
AB Title compds. [I; R = CH2CONHCH(CO2H)CH2CH2SH or the thiolactone thereof, CH2CONHASH, COASH, etc.; A = C1-20 linking group contg. 0-10 heteroatoms; R1 = H, Me, Ac, Et] are prepd. for coupling to a protein or polypeptide mol. (no data). Thus, morphine sulfate was condensed with BrCH2CO2H and the product condensed with D,L-homocysteine thiolactone to give I (R = CH2CONHR1, R1 = H, R3 = 2-oxo-3-tetrahydrothienyl).

IT **152904-93-3P 152904-95-5P 152904-96-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as hapten conjugate intermediate)

RN 152904-93-3 CAPLUS

CN Morphinan-17-acetamide, 7,8-didehydro-4,5-epoxy-6-ethoxy-3-hydroxy-N-(tetrahydro-2-oxo-3-thienyl)-, monohydrochloride, (5.alpha.,6.alpha.)-(9CI) (CA INDEX NAME)

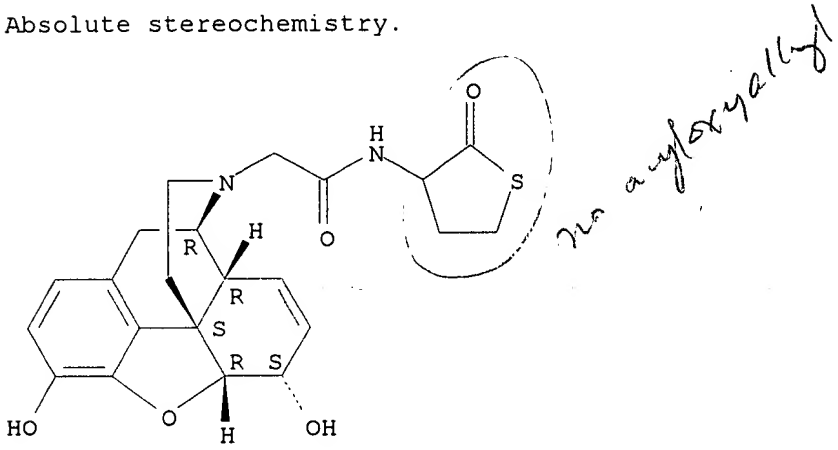
Absolute stereochemistry.



● HCl

RN 152904-95-5 CAPLUS
CN Morphinan-17-acetamide, 7,8-didehydro-4,5-epoxy-3,6-dihydroxy-N-(tetrahydro-2-oxo-3-thienyl)-, monohydrochloride, (5.alpha.,6.alpha.)-(9CI) (CA INDEX NAME)

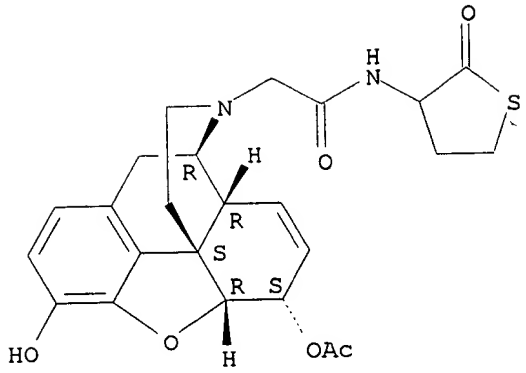
Absolute stereochemistry.



● HCl

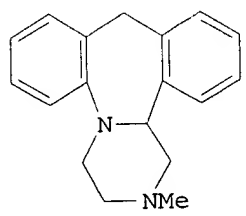
RN 152904-96-6 CAPLUS
CN Morphinan-17-acetamide,
6-(acetyloxy)-7,8-didehydro-4,5-epoxy-3-hydroxy-N-(tetrahydro-2-oxo-3-thienyl)-, monohydrochloride, (5.alpha.,6.alpha.)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

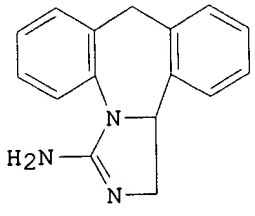


● HCl

L5 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1992:482892 CAPLUS
DN 117:82892
TI Chemical design of peripherally acting compounds
AU Jackson, W. Roy; Copp, Fred C.; Cullen, John D.; Guyett, Frances J.; Rae, Ian D.; Robinson, Andrea J.; Pothoulackis, Helen; Serelis, Algirdas K.; Wong, Margaret
CS Dep. Chem., Monash Univ., Melbourne, 3168, Australia
SO Clin. Exp. Pharmacol. Physiol. (1992), 19(1), 17-23
CODEN: CEXPB9; ISSN: 0305-1870
DT Journal
LA English
GI



I

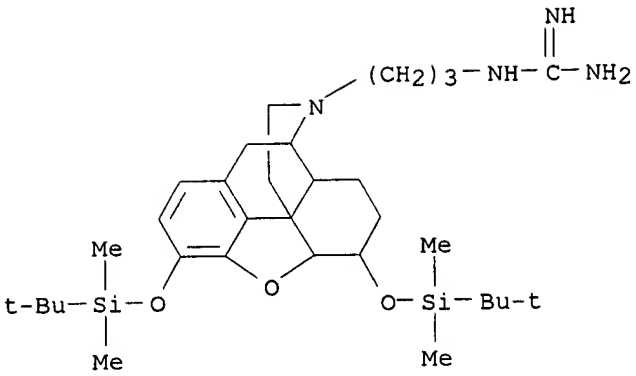


II

AB Some guanidines related in structure to mianserin (I) and WAL 801 (II) were synthesized and shown to be peripherally acting 5-HT2 antagonists. Structurally related compds. but not bearing a charged ionic group had central nervous system (CNS) activity. Computer-aided mol. modeling has been used to establish a 5-HT2 pharmacophore. The principle of exclusion from the CNS by incorporating a highly polar group to a biol. active mol. has been extended to the design and synthesis of a peripherally acting analgesic.

IT **142740-96-3P 142740-97-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and conversion to (aminoiminomethylaminopropyl)morphinan deriv.)

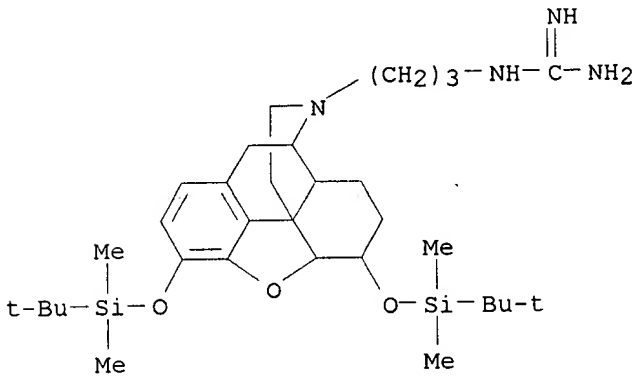
RN 142740-96-3 CAPLUS
CN Guanidine, [(5.alpha.,6.alpha.)-3-[3,6-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,5-epoxymorphinan-17-yl]propyl]- (9CI) (CA INDEX NAME)



RN 142740-97-4 CAPLUS
CN Guanidine, [(5.alpha.,6.alpha.)-3-[3,6-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,5-epoxymorphinan-17-yl]propyl]-, sulfate (1:1) (9CI) (CA INDEX NAME)

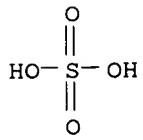
CM 1

CRN 142740-96-3
CMF C32 H56 N4 O3 Si2
CDES 4:5A,6A.MORPHINAN



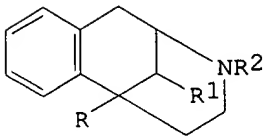
CM 2

CRN 7664-93-9
CMF H2 O4 S



L5 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1990:158025 CAPLUS
DN 112:158025
TI Synthesis of some N-acylaminoalkyl derivatives of 1,2,3,4,5,6-hexahydro-6-methyl- and 6,11-dimethyl-2,6-methano-3-benzazocine. I
AU Gutkowska, Bozenna; Rogala-Zawadzka, Grazyna; Ciszewski, Lech; Stefanowicz, Jacek

CS Inst. Drug. Sci., Sch. Med., Warsaw, 02-097, Pol.
SO Acta Pol. Pharm. (1988), 45(6), 478-85
CODEN: APPHAX; ISSN: 0001-6837
DT Journal
LA Polish
GI

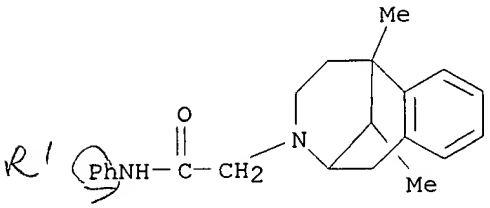


I

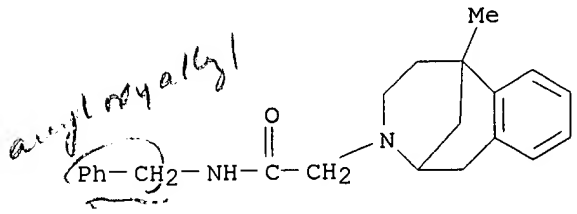
AB Treating benzazocine I (R = R1 = Me; R = Me, R1 = H; R2 = H) with BrCH2CO2Et gave 56, 75% I (same R, R1; R2 = CH2CO2Et) (II), resp. Subsequent treatment of II with amines gave 22-83% I (R2 = CH2CONHR3; R = R1 = Me, R3 = Ph; R = Me, R1 = H, R3 = 4-C6H4OMe, CH2Ph, hexyl) (III). Redn. of III with LiAlH4 in C6H6-Et2O gave 41-74% I (R = R1 = Me, R3 = Ph;
R = Me, R1 = H, R3 = CH2Ph, hexyl; R2 = CH2CH2NHR3), which were N-acylated
with (EtCO)2O in C6H6.

IT **126125-58-4P 126125-60-8P 126125-61-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and redn. of, with lithium aluminum hydride)

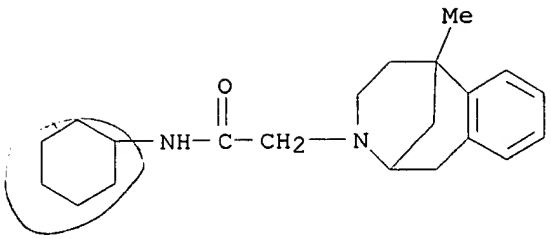
RN 126125-58-4 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-acetamide, 1,4,5,6-tetrahydro-6,11-dimethyl-N-phenyl- (9CI) (CA INDEX NAME)



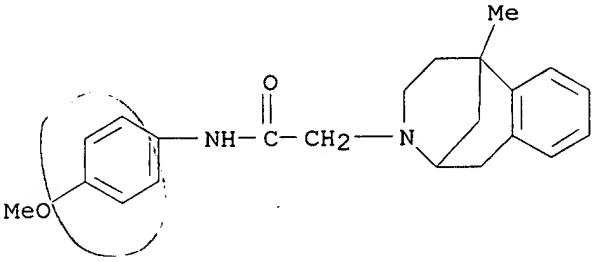
RN 126125-60-8 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-acetamide, 1,4,5,6-tetrahydro-6-methyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 126125-61-9 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-acetamide, N-cyclohexyl-1,4,5,6-tetrahydro-6-methyl- (9CI) (CA INDEX NAME)

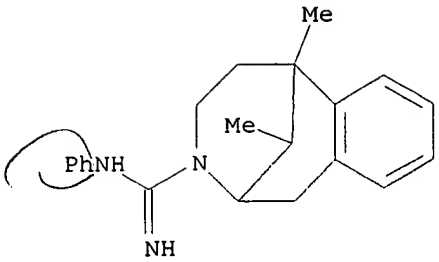


IT **126125-59-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 126125-59-5 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-acetamide, 1,4,5,6-tetrahydro-N-(4-methoxyphenyl)-6-methyl- (9CI) (CA INDEX NAME)



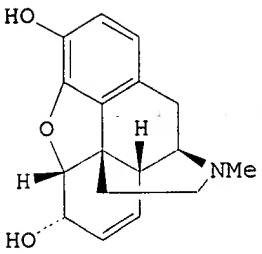
L5 ANSWER 12 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1990:111859 CAPLUS
Correction of: 1988:486100
DN 112:111859
Correction of: 109:86100
TI Biological evaluation of compounds for their physical dependence potential
and abuse liability. X. Drug testing programs of the Committee on Problems of Drug Dependence, Inc. (1986)
AU Jacobson, Arthur E.
CS Lab. Chem., Natl. Inst. Diabetes Dig. Kidney Dis., Bethesda, MD, 20892, USA
SO NIDA Res. Monogr. (1987), 76(Probl. Drug Depend., 1986), 370-91
CODEN: MIDAD4; ISSN: 0361-8595
DT Journal
LA English
AB A report is given on the drug-testing programs of the Committee on Problems of Drug Dependence, and new and lit. data are presented from studies of the dpendency potential of a large no. of drugs, including epoxymorphinans, phenylmorphans, benzomorphans, methadone-like compds., pethidines, fentanyls, etc.
IT **112239-63-1**
RL: PRP (Properties)
(abuse and dependence potential of)
RN 112239-63-1 CAPLUS
CN 2,6-Methano-3-benzazocine-3(4H)-carboximidamide, 1,2,5,6-tetrahydro-6,11-dimethyl-N-phenyl-, monohydrochloride, (2.alpha.,6.alpha.,11R*)- (9CI) (CA INDEX NAME)

Currently available stereo shown.



● HCl

L5 ANSWER 13 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1988:126022 CAPLUS
DN 108:126022
TI Development of fluoroimmunoassays for the specific detection of morphine in urine
AU Colbert, D. L.; Gallacher, G.; Ayling, P.; Turner, G. J.
CS Dep. Chem. Pathol., St. Bartholomew's Hosp., London, UK
SO Clin. Chim. Acta (1988), 171(1), 37-48
CODEN: CCATAR; ISSN: 0009-8981
DT Journal
LA English
GI



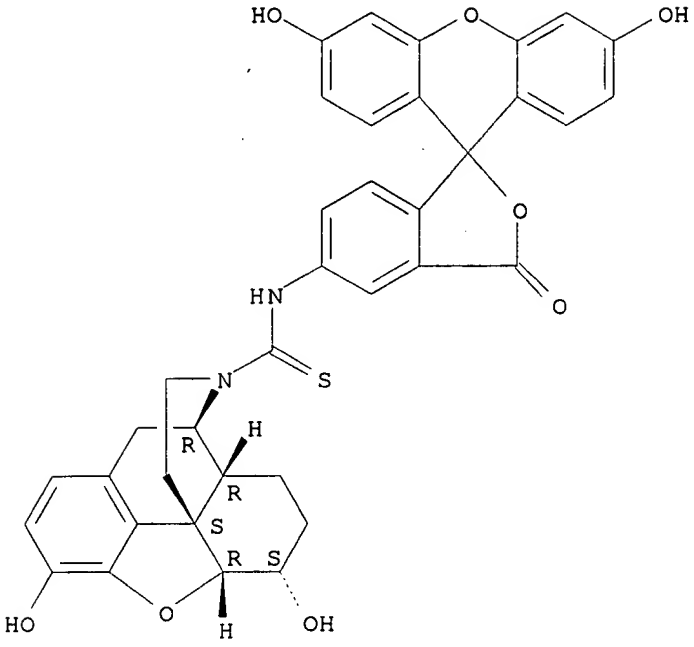
I

AB Two fluoroimmunoassays for the specific detection of morphine (I) in urine are described based on the use of ovine antibodies and fluorescein-labeled normorphine. The 1st, a polarization fluoroimmunoassay, is performed by adding 10 .mu.L of urine to 1.5 mL of a single-reagent, comprising premixed antiserum and tracer, incubation for a few minutes at ambient temp. and measurement of fluorescence polarization. The assay gives results which compare well with those by TLC, EMIT d.a.u., and the Boehringer opiate drug test. Although adequate for routine screening for drug abuse, the technique is not as sensitive as some radioimmunoassays. Therefore, a 2nd fluoroimmunoassay was developed based on the use of the same antibodies covalently coupled to magnetisable particles to facilitate both the sepn. of the bound and free fractions and the removal of nonspecific interfering substances. Thus, larger sample vols. could be employed and greater sensitivity achieved.

IT **113536-95-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as fluorscein-normorphine tracer, FIA in relation to)
RN 113536-95-1 CAPLUS
CN Morphinan-17-carbothioamide, N-(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)-4,5-epoxy-3,6-dihydroxy-, (5.alpha.,6.alpha.)-

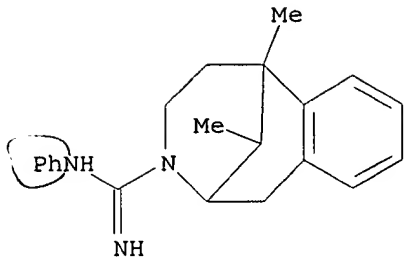
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 14 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1988:106303 CAPLUS
DN 108:106303
TI Dependence studies of new compounds in the rhesus monkey, rat and mouse (1986)
AU Aceto, M. D.; Bowman, E. R.; Harris, L. S.; May, E. L.
CS USA
SO NIDA Res. Monogr. (1987), 76(Probl. Drug Depend., 1986), 392-447
CODEN: MIDAD4; ISSN: 0361-8595
DT Journal
LA English
AB Data are presented on the ability of a large no. of drugs to substitute for morphine in a variety of drug dependence-withdrawal models in mice, rats, and monkeys.
IT **112239-63-1**, NIH 10253
RL: BIOL (Biological study)
(dependence on, potential for)
RN 112239-63-1 CAPLUS
CN 2,6-Methano-3-benzazocine-3(4H)-carboximidamide, 1,2,5,6-tetrahydro-6,11-dimethyl-N-phenyl-, monohydrochloride, (2.alpha.,6.alpha.,11R*)- (9CI) (CA INDEX NAME)

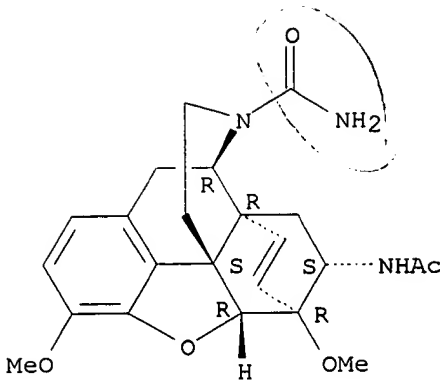
Currently available stereo shown.



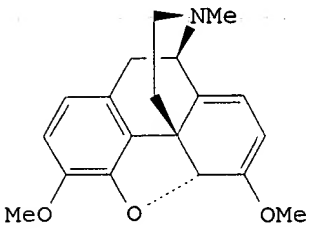
● HCl

L5 ANSWER 15 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1986:583740 CAPLUS
DN 105:183740
TI Probes for narcotic receptor mediated phenomena. 13. Potential irreversible narcotic antagonist-based ligands derived from 6,14-endo-ethenotetrahydrooripavine with 7-(methoxyfumaroyl)amino, (bromoacetyl)amino, or isothiocyanate electrophiles: chemistry, biochemistry, and pharmacology
AU Lessor, Ralph A.; Bajwa, Balbir S.; Rice, Kenner C.; Jacobson, Arthur E.; Streaty, Richard A.; Klee, Werner A.; Smith, Charles B.; Aceto, Mario D.; May, Everette L.; Harris, Louis S.
CS Lab. Chem., Natl. Inst. Arthritis, Diabetes, Dig. Kidney Dis., Bethesda, MD, 20892, USA
SO J. Med. Chem. (1986), 29(11), 2136-41
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
GI For diagram(s), see printed CA Issue.
AB A series of 12 title compds. [I; R = 2-propenyl, Pr, cyclopropylmethyl; R1 = H, isothiocyanato, (bromoacetyl)amino, or (methoxyfumaroyl)amino] were prepd., starting from 7.alpha.-(acetylamino)-6,14-endo-ethenotetrahydrothebaine [24485-07-2], and tested for narcotic-agonist and -antagonist activities and their ability to interact with opioid receptors in vitro. All I were reasonably potent narcotic antagonists in the morphine-induced tail-flick assay in mice. The N-(cyclopropylmethyl)-substituted I, however, had the highest affinity for rat brain opioid receptors; the potency was 0.017-0.5 times that of morphine. Only 2 of the cyclopropylmethyl-substituted I, among all the compds. studied, were bound irreversibly and selectively with (.mu.- or .delta.-opioid receptors of NG108-15 neuroblastoma-glioma cells; these same I were also bound irreversibly to .kappa.-opioid receptors, whereas neither compd. showed irreversible action in the elec. stimulated mouse vas deferens prepn.
IT **102779-80-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and nitrite-promoted hydrolysis and decarboxylation of)
RN 102779-80-6 CAPLUS
CN 6,14-Ethenomorphinan-17-carboxamide, 7-(acetylamino)-4,5-epoxy-3,6-dimethoxy-, (5.alpha.,7.alpha.)- (9CI) (CA INDEX NAME)

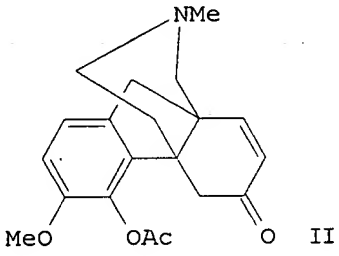
Absolute stereochemistry.



L5 ANSWER 16 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1985:422818 CAPLUS
DN 103:22818
TI Lateral control of skeletal rearrangement by complexation of thebaine with
iron tricarbonyl (Fe(CO)3)
AU Birch, A. J.; Kelly, L. F.; Liepa, A. J.
CS Dep. Chem., Aust. Natl. Univ., Canberra, 2601, Australia
SO Tetrahedron Lett. (1985), 26(4), 501-4
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
OS CASREACT 103:22818
GI



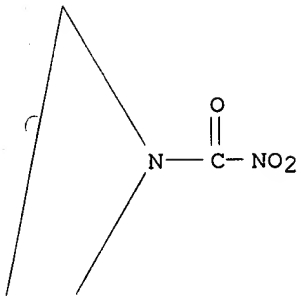
I

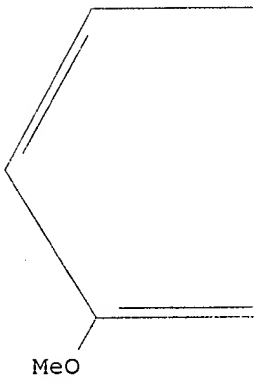


II

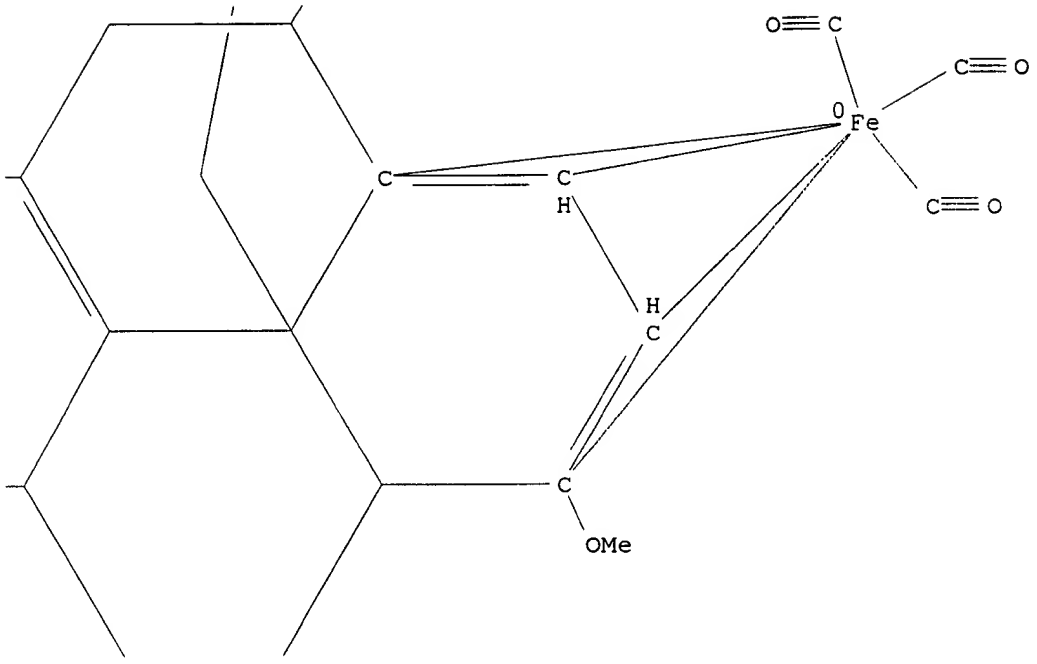
AB Temporary attachment of Fe(CO)3 to thebaine (I) allows access to northebaine, 14.alpha.-substituted thebainone derivs., and a rearranged codeinone analog II lacking the oxide ring and in which the dihydrophenanthrene nucleus is replaced by a dihydrofluorene one.

IT **96743-83-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and decomplexation of)
RN 96743-83-8 CAPLUS
CN Iron, tricarbonyl[(6,7,8,14-.eta.)-(5.alpha.)-6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-.alpha.-nitromorphinan-17-carboxaldehyde]-, stereoisomer (9CI) (CA INDEX NAME)

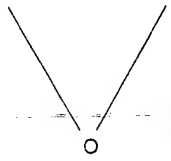

O
N
C
NO2


MeO

PAGE 2-B

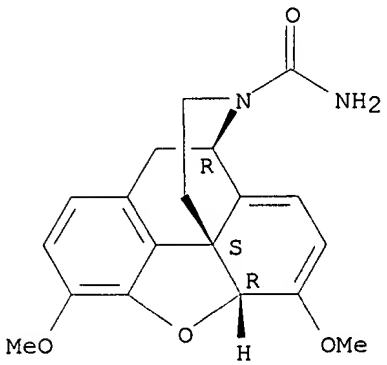


PAGE 3-B



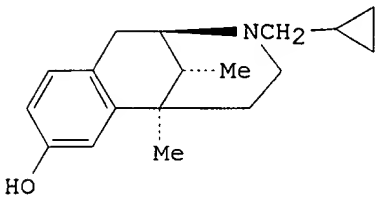
IT **96860-96-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 96860-96-7 CAPLUS
CN Morphinan-17-carboxamide, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-, (5.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 17 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1981:400113 CAPLUS

DN 95:113
TI Radioimmunoassay of cyclazocine and stereospecificity of antibody
AU Maeda, Masako; Tsuji, Akio
CS Sch. Pharm. Sci., Showa Univ., Tokyo, Japan
SO J. Pharmacobio-Dyn. (1981), 4(3), 167-74
CODEN: JOPHDQ; ISSN: 0386-846X
DT Journal
LA English
GI



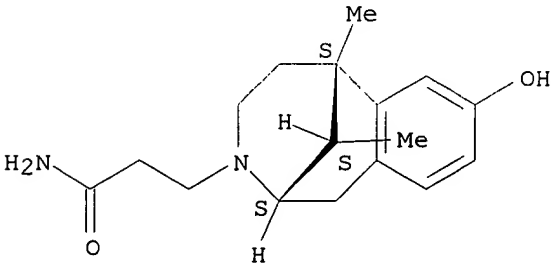
I

AB A new radioimmunoassay, using 3H-labeled dl-cyclazocine (I) [7346-09-0] rabbit antiserum and charcoal-dextran sepn. of bound and free cyclazocine, for the direct anal. of serum cyclazocine is described. This method, which is specific for cyclazocine and has a detection limit of .apprx.25 pg/assay tube, was successful in detg. the cyclazocine level in the sera of dogs injected i.m. with 3 or 10 .mu.g/kg cyclazocine. The drug half-life was 90 min; the apparent distribution vols. were 4.0 and 5.26 L/kg, resp. One of the antisera from rabbits immunized with dl-cyclazocin deriv.-bovine serum albumin conjugate was highly sp. for l-cyclazocine [7313-86-2].

IT **77943-85-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, antibody formation in radioimmunoassay for cyclazocine in relation to)

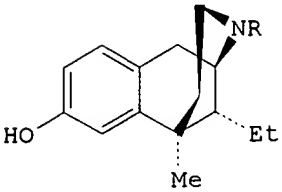
RN 77943-85-2 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-propanamide, 1,4,5,6-tetrahydro-8-hydroxy-6,11-dimethyl-, (2.alpha.,6.alpha.,11R*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

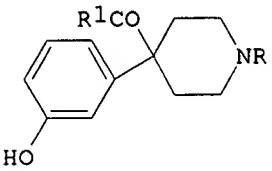


L5 ANSWER 18 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1979:449269 CAPLUS
DN 91:49269
TI N-(2-Cyanoethyl) derivatives of meperidine, ketobemidone, and a potent 6,7-benzomorphan
AU Uwaydah, Ibrahim M.; Waddle, M. Kathleen; Rogers, Michael E.
CS Med. Coll. Virginia, Virginia Commonwealth Univ., Richmond, VA, 23298, USA

SO J. Med. Chem. (1979), 22(7), 889-90
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
GI



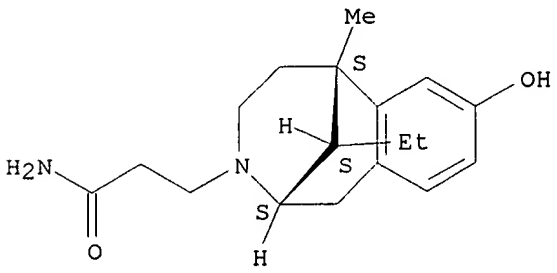
I



II

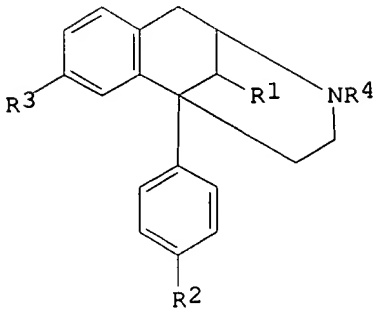
AB The cyanoethyl and carbamido derivs. of the benzomorphan I (R = CH2CH2CN, CH2CH2CONH2) and the cyanoethyl derivs. of meperidine and ketobemidone II (R CH2CH2CN; R1 = OEt, Et) were prepd. by alkylation of the resp. norbase with acrylonitrile and acrylamide and evaluated for analgesic activity in the hot-plate assay and for receptor affinity.
2-(2-Cyanoethyl)-9.alpha.-
ethyl-2'-hydroxy-5-methyl-6,7-benzomorphan [70570-52-4] was 6 times more potent than its N-Me parent and showed a corresponding increase in receptor affinity; it did not show antagonistic activity in the
tail-flick
assay, and in single-dose suppression test substituted briefly for morphine. The activity of the N-2-cyanoethyl substituent is apparently dependent on the parent opiate. Structure activity relations are discussed.
IT **70650-78-1P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and analgesic activity of)
RN 70650-78-1 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-propanamide,
11-ethyl-1,4,5,6-tetrahydro-8-
hydroxy-6-methyl-, (2.alpha.,6.alpha.,11R*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L5 ANSWER 19 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1979:432642 CAPLUS
DN 91:32642
TI Syntheses, analgetic activity and physical dependence capacity of 5-phenyl-6,7-benzomorphan derivatives
AU Yokoyama, Naokata; Almaula, Prabodh I.; Block, Fred B.; Granat, Frank R.; Gottfried, Norman; Hill, Ronald T.; McMahon, Elihu H.; Munch, Walter F.; Rachlin, Howard; et al.
CS Pharm. Div., Ciba-Geigy Corp., Ardsley, NY, USA

SO J. Med. Chem. (1979), 22(5), 537-53
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
GI

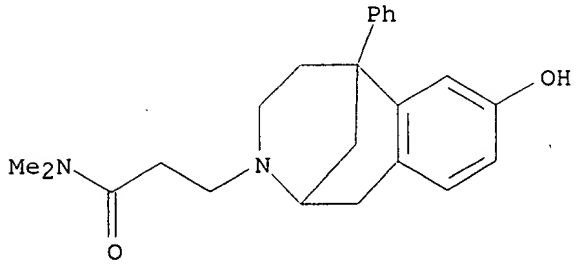


I

AB The title compds. I (R1 = H, Me, Et; R2 = H, Cl, F, OH, OAc; R3 = H, F, OH, Ac, OAc, OMe, etc.; R4 = H, CN, CO2Et, Me) were prepd. by generalized procedures from 4-piperidinones via Stevens rearrangement, followed by cyclization of the obtained product. The Stevens rearrangement products (4-aryl-2-benzyl-.DELTA.3-piperidine derivs.) and I were evaluated for analgesic effect and phys. dependence capacities in mice. The abs. configuration of I was established by comparison of their ORD and CD spectra of a known benzomorphan. Among the piperidine derivs. 2-benzyl-1-methyl-4-phenyl-.DELTA.3-piperidine-HBr [18136-06-6] and among
I 1-2'-hydroxy-9.beta.-methyl-2-pentyl-5-phenyl-6,7-benzomorphan [70257-23-7] were the most potent analgesics. Structure-activity relations are discussed.

IT **70256-52-9P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and analgesic activity of)

RN 70256-52-9 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-propanamide, 1,4,5,6-tetrahydro-8-hydroxy-N,N-dimethyl-6-phenyl- (9CI) (CA INDEX NAME)



L5 ANSWER 20 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1979:103862 CAPLUS
DN 90:103862
TI Imidazolylmethyl methanobenzazocines
IN Albertson, Noel F.
PA Sterling Drug, Inc., USA
SO U.S., 12 pp.
CODEN: USXXAM

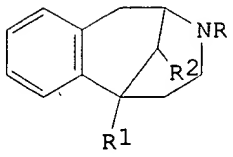
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4108857	A	19780822	US 1977-772984	19770228
				US 1964-405244	19641020
				US 1967-642224	19670529
				US 1969-856157	19690908
				US 1971-133400	19710412
				US 1975-605272	19750818
	US 3382249	A	19680507	US 1964-405244	19641020

PATENT FAMILY INFORMATION:
FAN 1968:496509

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3382249	A	19680507	US 1964-405244	19641020
	US 4108857	A	19780822	US 1977-772984	19770228
				US 1964-405244	19641020
				US 1967-642224	19670529
				US 1969-856157	19690908
				US 1971-133400	19710412
				US 1975-605272	19750818

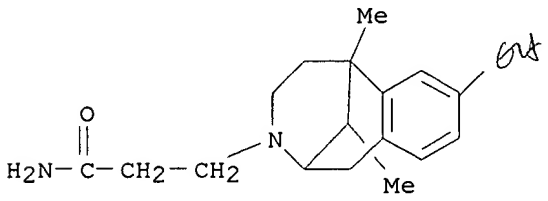
GI



I

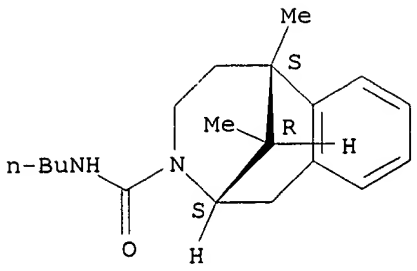
AB Methanobenzazocines I (R = 1-alkyl-5-imidazolylmethyl; R1 = alkyl; R2 = H, alkyl) were prepd. Thus, I (R = 1-methyl-5-imidazolylmethyl, R1 = R2 = Me) was obtained by treating I (R = H, R1 = R2 = Me) with 1-methyl-5-chloromethylimidazole-HCl. I (R = cyclopropylmethyl, R1 = R2 = Me) was also prepd. and had anticonvulsant, central nervous system depressant, and diuretic activity. Some I had muscle relaxant activity.

IT **69336-03-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and redn. of)
RN 69336-03-4 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-propanamide, 1,4,5,6-tetrahydro-6,11-dimethyl-, (2.alpha.,6.alpha.,11S*)- (9CI) (CA INDEX NAME)



IT **69336-08-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 69336-08-9 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide, N-butyl-1,4,5,6-tetrahydro-6,11-dimethyl-, (2.alpha.,6.alpha.,11S*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

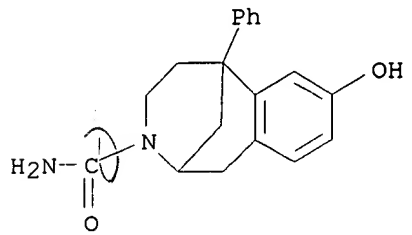


L5 ANSWER 21 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1977:551868 CAPLUS
DN 87:151868
TI Urea derivatives
IN Yamamoto, Michihiro; Koshiba, Masao; Yamamoto, Hisao
PA Sumitomo Chemical Co., Ltd., Japan
SO Japan. Kokai, 7 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 52073801	A2	19770621	JP 1975-151617	19751217
	JP 59008272	B4	19840223		

AB Sixty-five urea derivs. RR1NCONR2R3 (R = alkyl, cycloalkyl, aralkyl, adamantyl, aryl, heterocyclic; R1 = H, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl; RNR1 may form a ring; R2 = H, alkyl, alkenyl, cycloalkyl, aralkyl, alkoxy; R3 = H, alkyl, alkenyl; R2NR3 may form a ring) were prepd. by reaction of RR1NH with X3CCO2H (X = halo) or their derivs. followed by reaction of the resulting RR1NCOCX3 with R2R3NH. Thus, 10 g Et3N was added to a mixt. of 12.8 g 4-ClC6H4NH2 and 18.2 g Cl3CCOCl in C6H6 with ice cooling and the whole stirred 5 h at room temp. to give 86% 4-ClC6H4NHCOCCl3 (I). Autoclaving 1.37 g I with 3 g NH3 at room temp. overnight gave 94% 4-ClC6H4NHCONH2.

IT **5099-78-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 5099-78-5 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide, 1,4,5,6-tetrahydro-8-hydroxy-6-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



L5 ANSWER 22 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1976:587540 CAPLUS
DN 85:187540

TI Spin labeled compounds for use in forensic analysis
IN Goldstein, Avram; Leute, Richard K.; Ullman, Edwin F.
PA Syva Co., USA
SO U.S., 46 pp. Continuation of U.S. 3,853,914.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3966744	A	19760629	US 1974-482542	19740624
				US 1971-105535	19710111
				US 1971-141516	19710510
				US 1972-270108	19720710
	US 3690834	A	19720912	US 1971-141516	19710510
	FR 2121723	A5	19720825	FR 1972-687	19720110
	FR 2121723	B1	19730629		
				US 1971-105535	19710111
	US 3853914	A	19741210	US 1972-270108	19720710
				US 1971-105535	19710111
				US 1971-141516	19710510

PATENT FAMILY INFORMATION:
FAN 1973:93406

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2201165	A	19720803	DE 1972-2201165	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510
	US 3690834	A	19720912	US 1971-141516	19710510
	IL 38517	A1	19751015	IL 1972-38517	19720106
				US 1971-105535	19710111
				US 1971-141516	19710510
	NL 7200316	A	19720713	NL 1972-316	19720110
				US 1971-105535	19710111
				US 1971-141516	19710510
	FR 2121723	A5	19720825	FR 1972-687	19720110
	FR 2121723	B1	19730629		
				US 1971-105535	19710111
	CH 580810	A	19761015	CH 1972-308	19720110
				US 1971-105535	19710111
				US 1971-141516	19710510
	GB 1385342	A	19750226	GB 1972-1313	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510
	GB 1385343	A	19750226	GB 1974-33210	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510
	CA 1012131	A1	19770614	CA 1972-132163	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510

FAN 1975:453630

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2264742	A1	19741031	DE 1972-2264742	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510
	US 3690834	A	19720912	US 1971-141516	19710510
	IL 38517	A1	19751015	IL 1972-38517	19720106
				US 1971-105535	19710111
				US 1971-141516	19710510
	NL 7200316	A	19720713	NL 1972-316	19720110
				US 1971-105535	19710111
				US 1971-141516	19710510
	FR 2121723	A5	19720825	FR 1972-687	19720110
	FR 2121723	B1	19730629		

				US 1971-105535	19710111
	CH 580810	A	19761015	CH 1972-308	19720110
				US 1971-105535	19710111
				US 1971-141516	19710510
	GB 1385342	A	19750226	GB 1972-1313	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510
	GB 1385343	A	19750226	GB 1974-33210	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510
	CA 1012131	A1	19770614	CA 1972-132163	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510

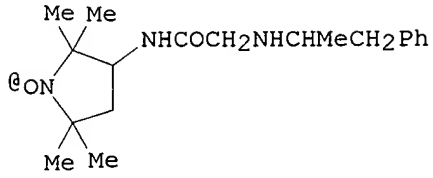
FAN 1976:538340

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3959287	A	19760525	US 1974-466650	19740503
				US 1971-105535	19710111
				US 1971-141516	19710510
				US 1972-270108	19720710
	US 3690834	A	19720912	US 1971-141516	19710510
	FR 2121723	A5	19720825	FR 1972-687	19720110
	FR 2121723	B1	19730629		
				US 1971-105535	19710111
	US 3853914	A	19741210	US 1972-270108	19720710
				US 1971-105535	19710111
				US 1971-141516	19710510

FAN 1976:538341

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3966764	A	19760629	US 1974-482200	19740624
				US 1972-270108	19720710
	US 3853914	A	19741210	US 1972-270108	19720710
				US 1971-105535	19710111
				US 1971-141516	19710510

GI



II

AB Spin labeled compds. (ligand analogs) for use in forensic immunoassay were prepd. by modifying biol. active compds. or structural analogs and coupling them with a stable free radical compd. The ligand analog is recognizable by receptor mol., usually on antibody, and can compete with a biol. active mol. (ligand) for the receptor site in a way which allows the biol. active mol. to be assayed spectrometrically. For example, 2 mmoles amphetamine (I) [300-62-9] in 20 ml MeOH was treated with 106 mg Na2CO3 [497-19-8] and 321 mg 3-(2'-iodoacetamido)-2,2,5,5-tetramethyl-1-pyrrolidinyl-1-oxyl [27048-01-7] to give 187 mg 3-(N-(1'-phenyl-2'-propyl)glycinamido)-2,2,5,5-tetramethylpyrrolidinyl-1-oxyl (II) [41370-71-2]. The Et2O ext. of a soln. of 3.68 g amphetamine sulfate [60-13-9] in 80 ml 0.5N NaOH was evapd., and the residue was dissolved in 50 ml benzene and treated with 3 ml diisopropylethylamine [7087-68-5] and

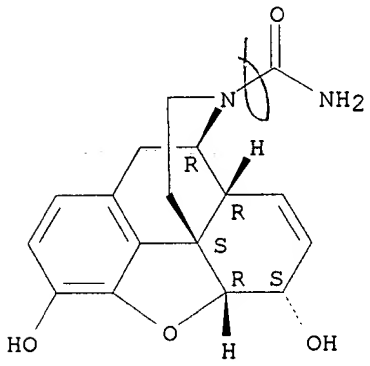
2.2 ml Et bromoacetate [105-36-2] to give the amino ester. The ester was dissolved in 50 ml 1:1 MeOH-1N NaOH, and the soln. was concd., and treated with HCl to pH 6 to give 900 mg N-carboxymethyl amphetamine [7738-39-8]. A suspension of the acid (700 mg) in 50 ml dry dioxane was treated with 20 ml of 12.5% phosgene in benzene, and the mixt. was evapd., redissolved in 20 ml/dry dioxane, and added over .5 hr to 2 g bovine serum albumin in 100 ml 2% NaHCO3 at 0.degree.. After 24 hr at 0.degree. and 18 hr at room temp., the reaction mixt. was dialyzed for 2 days against 35 l H2O at 0.degree., and lyophilized, giving 1.91 g conjugate contg. .apprx.76 I units per unit of albumin. For urine anal. for I, 25 .mu.l urine was mixed with 2.5 .mu.l 0.2M Na2Cr2O7 and added to a mixt. of 22 .mu.l I antibody (.gamma.-globulin), 144 .mu.l 2M pH8 borate buffer, and 99 .mu.l saline. Five .mu.l of a soln. of 105 .mu.l H2O and 160 .mu.l 2.8 .times. 10-5M I soln. was added, and the soln. was examd. by ESR spectroscopy. The method detected I concns. in the range of 0.7-1.5 .mu.g/ml. It also detected several other drugs with structures similar to I.

IT **56740-96-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and decarbamoylation of)

RN 56740-96-6 CAPLUS

CN Morphinan-17-carboxamide, 7,8-didehydro-4,5-epoxy-3,6-dihydroxy-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 23 OF 37 CAPLUS COPYRIGHT 2001 ACS

AN 1976:577722 CAPLUS

DN 85:177722

TI Thiourea derivatives in the morphine group, I

AU Bognar, Rezso; Gaal, Gyorgy; Kerekes, Peter; Horvath, Geza; Szikszai, Eszter

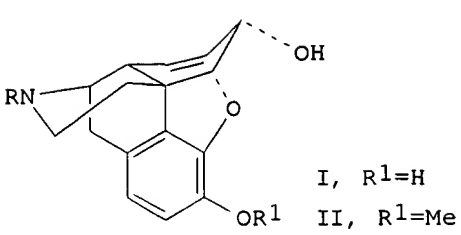
CS Dep. Org. Chem., Kossuth Lajos Univ., Debrecen, Hung.

SO Acta Chim. Acad. Sci. Hung. (1976), 89(1), 55-60
CODEN: ACASA2

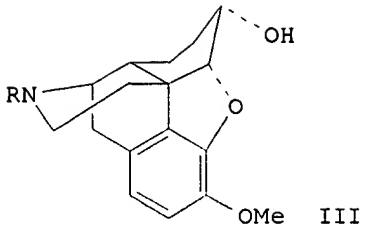
DT Journal

LA English

GI



I, R^1=H
II, R^1=Me



III

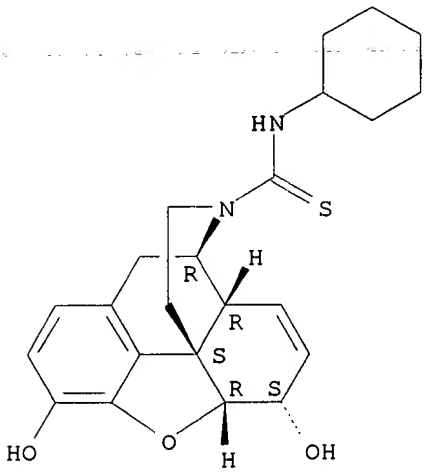
AB The normophines I (R = PhCH2NHCS, cyclohexylthiocarbamoyl), norcodeines II
(R = MeNHCS, PhNHCS, PhCH2NHCS, cyclohexylthiocarbamoyl, 2,3,4,6-tetraacetyl-.beta.-D-glucosylthiocarbamoyl), and dihydronorcodeines III (R = MeNHCS, PhNHCS, cyclohexylthiocarbamoyl, 2,3,4,6-tetraacetyl-.beta.-D-glucosylthiocarbamoyl and 1-adamantylthiocarbamoyl) were prepd. by treating I, II, III (R = H) with isothiocyanates.

IT **60888-46-2P 60888-47-3P 60888-48-4P**
60888-49-5P 60888-50-8P 60888-51-9P
60888-52-0P 60888-53-1P 60888-54-2P
60888-55-3P 60888-56-4P 60888-57-5P
60908-97-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 60888-46-2 CAPLUS

CN Morphinan-17-carbothioamide, N-cyclohexyl-7,8-didehydro-4,5-epoxy-3,6-dihydroxy-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

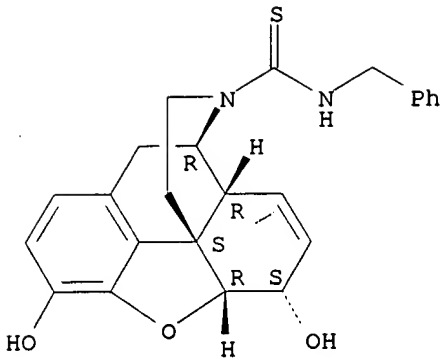
Absolute stereochemistry.



RN 60888-47-3 CAPLUS

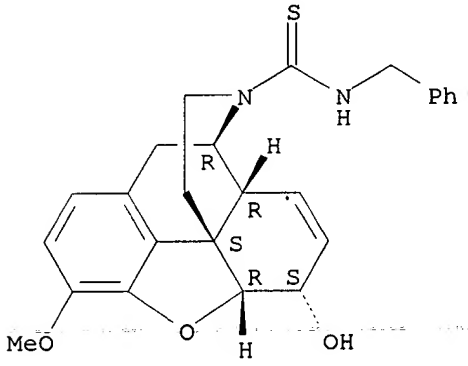
CN Morphinan-17-carbothioamide, 7,8-didehydro-4,5-epoxy-3,6-dihydroxy-N-(phenylmethyl)-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



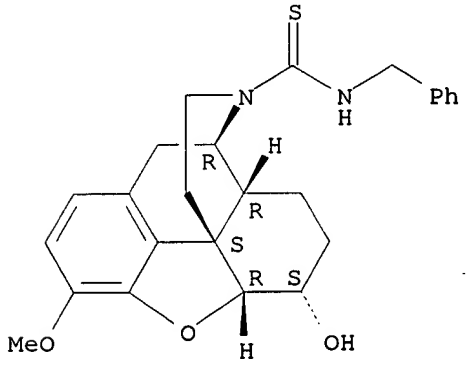
RN 60888-48-4 CAPLUS
CN Morphinan-17-carbothioamide,
7,8-didehydro-4,5-epoxy-6-hydroxy-3-methoxy-N-
(phenylmethyl)-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



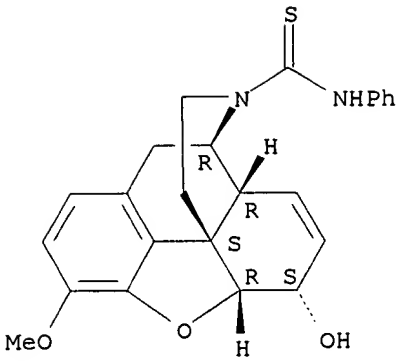
RN 60888-49-5 CAPLUS
CN Morphinan-17-carbothioamide, 4,5-epoxy-6-hydroxy-3-methoxy-N-
(phenylmethyl)-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



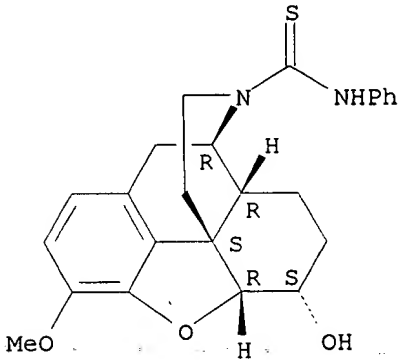
RN 60888-50-8 CAPLUS
CN Morphinan-17-carbothioamide,
7,8-didehydro-4,5-epoxy-6-hydroxy-3-methoxy-N-
phenyl-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



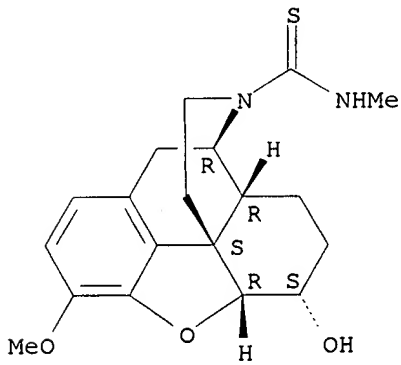
RN 60888-51-9 CAPLUS
CN Morphinan-17-carbothioamide, 4,5-epoxy-6-hydroxy-3-methoxy-N-phenyl-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



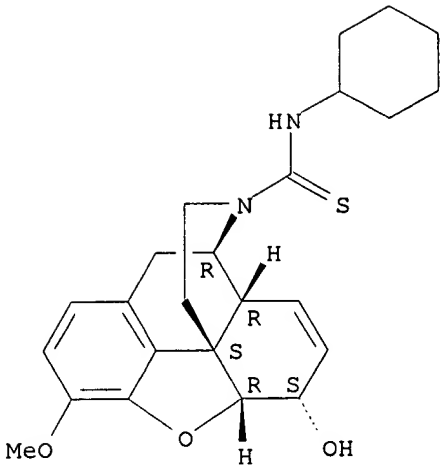
RN 60888-52-0 CAPLUS
CN Morphinan-17-carbothioamide, 4,5-epoxy-6-hydroxy-3-methoxy-N-methyl-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



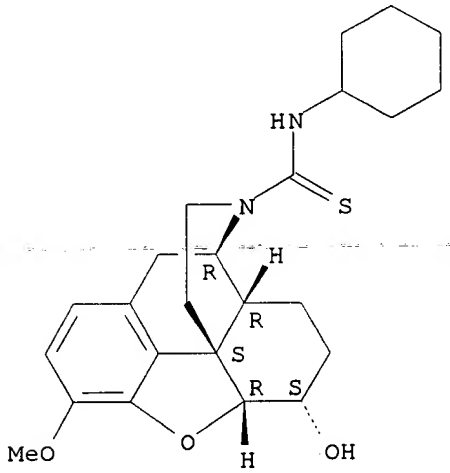
RN 60888-53-1 CAPLUS
CN Morphinan-17-carbothioamide, N-cyclohexyl-7,8-didehydro-4,5-epoxy-6-hydroxy-3-methoxy-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

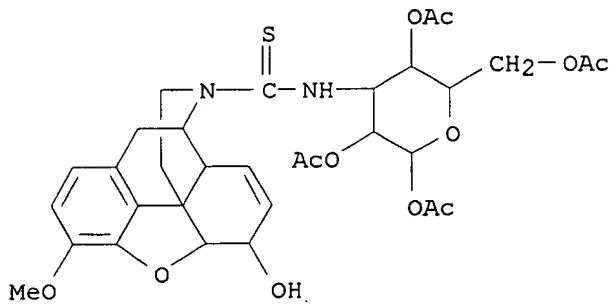


RN 60888-54-2 CAPLUS
CN Morphinan-17-carbothioamide, N-cyclohexyl-4,5-epoxy-6-hydroxy-3-methoxy-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

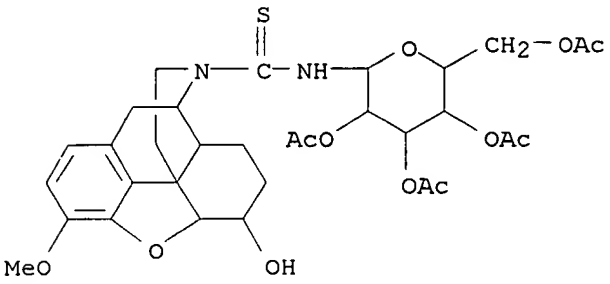


RN 60888-55-3 CAPLUS
CN Morphinan-17-carbothioamide, 7,8-didehydro-4,5-epoxy-6-hydroxy-3-methoxy-N-(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)



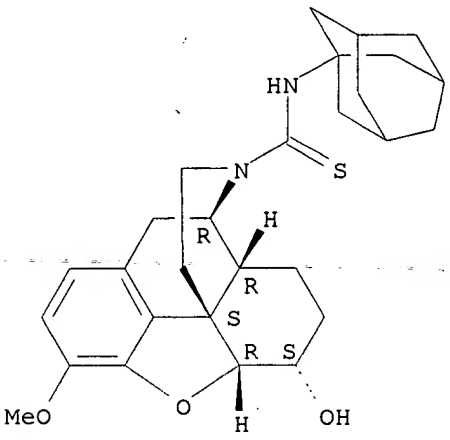
RN 60888-56-4 CAPLUS

CN Morphinan-17-carbothioamide, 4,5-epoxy-6-hydroxy-3-methoxy-N-(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)



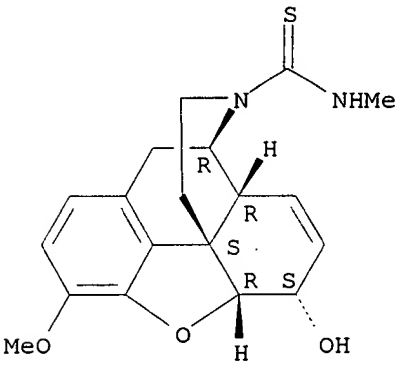
RN 60888-57-5 CAPLUS
CN Morphinan-17-carbothioamide, 4,5-epoxy-6-hydroxy-3-methoxy-N-tricyclo[3.3.1.13,7]dec-1-yl-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 60908-97-6 CAPLUS
CN Morphinan-17-carbothioamide, 7,8-didehydro-4,5-epoxy-6-hydroxy-3-methoxy-N-methyl-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 24 OF 37 CAPLUS COPYRIGHT 2001 ACS

AN 1976:538341 CAPLUS
DN 85:138341
TI Ligand determination of spin labeled compounds by receptor displacement-amphetamine analogs
IN Goldstein, Avram; Leute, Richard K.; Ullman, Edwin F.
PA Syva Co., USA
SO U.S., 45 pp. Division of U.S. 3,853,914.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3966764	A	19760629	US 1974-482200	19740624
				US 1972-270108	19720710
	US 3853914	A	19741210	US 1972-270108	19720710
				US 1971-105535	19710111
				US 1971-141516	19710510

PATENT FAMILY INFORMATION:

FAN 1973:93406

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2201165	A	19720803	DE 1972-2201165	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510
	US 3690834	A	19720912	US 1971-141516	19710510
	IL 38517	A1	19751015	IL 1972-38517	19720106
				US 1971-105535	19710111
				US 1971-141516	19710510
	NL 7200316	A	19720713	NL 1972-316	19720110
				US 1971-105535	19710111
				US 1971-141516	19710510
	FR 2121723	A5	19720825	FR 1972-687	19720110
	FR 2121723	B1	19730629		
				US 1971-105535	19710111
	CH 580810	A	19761015	CH 1972-308	19720110
				US 1971-105535	19710111
				US 1971-141516	19710510
	GB 1385342	A	19750226	GB 1972-1313	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510
	GB 1385343	A	19750226	GB 1974-33210	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510
	CA 1012131	A1	19770614	CA 1972-132163	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510

FAN 1975:453630

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2264742	A1	19741031	DE 1972-2264742	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510
	US 3690834	A	19720912	US 1971-141516	19710510
	IL 38517	A1	19751015	IL 1972-38517	19720106
				US 1971-105535	19710111
				US 1971-141516	19710510
	NL 7200316	A	19720713	NL 1972-316	19720110
				US 1971-105535	19710111
				US 1971-141516	19710510
	FR 2121723	A5	19720825	FR 1972-687	19720110
	FR 2121723	B1	19730629		
				US 1971-105535	19710111
	CH 580810	A	19761015	CH 1972-308	19720110
				US 1971-105535	19710111

				US 1971-141516	19710510
	GB 1385342	A	19750226	GB 1972-1313	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510
	GB 1385343	A	19750226	GB 1974-33210	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510
	CA 1012131	A1	19770614	CA 1972-132163	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510

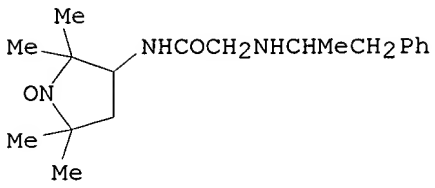
FAN 1976:538340

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3959287	A	19760525	US 1974-466650	19740503
				US 1971-105535	19710111
				US 1971-141516	19710510
				US 1972-270108	19720710
	US 3690834	A	19720912	US 1971-141516	19710510
	FR 2121723	A5	19720825	FR 1972-687	19720110
	FR 2121723	B1	19730629		
				US 1971-105535	19710111
	US 3853914	A	19741210	US 1972-270108	19720710
				US 1971-105535	19710111
				US 1971-141516	19710510

FAN 1976:587540

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3966744	A	19760629	US 1974-482542	19740624
				US 1971-105535	19710111
				US 1971-141516	19710510
				US 1972-270108	19720710
	US 3690834	A	19720912	US 1971-141516	19710510
	FR 2121723	A5	19720825	FR 1972-687	19720110
	FR 2121723	B1	19730629		
				US 1971-105535	19710111
	US 3853914	A	19741210	US 1972-270108	19720710
				US 1971-105535	19710111
				US 1971-141516	19710510

GI



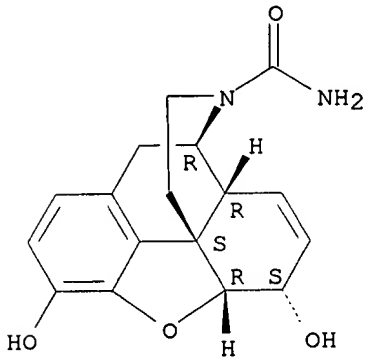
I

AB Biol. active compds. or structural analogs are coupled with a stable free radical compd. to give a ligand analog which is recognized by a receptor mol., ordinarily an antibody, and can compete for the receptor site in a manner to permit detn. of the biol. active compd. Changes in ESR spectrum between ligand analog bound to receptor and unbound ligand analog free in soln. permit quant. detn. of the amt. of biol. active ligand in the soln. Thus, an amphetamine antibody prepd. using N-(carboxymethyl)amphetamine [7738-39-8]-bovine serum albumin conjugate and spin labeled analog 3-[N-(1'-phenyl-2'-propyl)glycinamido]-2,2,5,5-tetramethylpyrrolidinyl-1-oxyl (I) [41370-71-2] were used in the detn. of amphetamine [300-62-9] in urine. Several examples of spin labeled analogs of drugs, opiates, and steroids are given.

IT **56740-96-6P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and decarbamolyation of)
RN 56740-96-6 CAPLUS
CN Morphinan-17-carboxamide, 7,8-didehydro-4,5-epoxy-3,6-dihydroxy-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 25 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1976:538340 CAPLUS
DN 85:138340
TI Ligand determination of spin labeled compounds by receptor displacement
IN Goldstein, Avram; Leute, Richard K.; Ullman, Edwin F.
PA Syva Co., USA
SO U.S., 19 pp. Division of U.S. 3,853,914.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3959287	A	19760525	US 1974-466650	19740503
				US 1971-105535	19710111
				US 1971-141516	19710510
				US 1972-270108	19720710
	US 3690834	A	19720912	US 1971-141516	19710510
	FR 2121723	A5	19720825	FR 1972-687	19720110
	FR 2121723	B1	19730629		
				US 1971-105535	19710111
	US 3853914	A	19741210	US 1972-270108	19720710
				US 1971-105535	19710111
				US 1971-141516	19710510

PATENT FAMILY INFORMATION:
FAN 1973:93406

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2201165	A	19720803	DE 1972-2201165	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510
	US 3690834	A	19720912	US 1971-141516	19710510
	IL 38517	A1	19751015	IL 1972-38517	19720106
				US 1971-105535	19710111
				US 1971-141516	19710510
	NL 7200316	A	19720713	NL 1972-316	19720110
				US 1971-105535	19710111
				US 1971-141516	19710510
	FR 2121723	A5	19720825	FR 1972-687	19720110
	FR 2121723	B1	19730629		
				US 1971-105535	19710111

	CH 580810	A	19761015	CH 1972-308	19720110
				US 1971-105535	19710111
				US 1971-141516	19710510
	GB 1385342	A	19750226	GB 1972-1313	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510
	GB 1385343	A	19750226	GB 1974-33210	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510
	CA 1012131	A1	19770614	CA 1972-132163	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510

FAN 1975:453630

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2264742	A1	19741031	DE 1972-2264742	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510
	US 3690834	A	19720912	US 1971-141516	19710510
	IL 38517	A1	19751015	IL 1972-38517	19720106
				US 1971-105535	19710111
				US 1971-141516	19710510
	NL 7200316	A	19720713	NL 1972-316	19720110
				US 1971-105535	19710111
				US 1971-141516	19710510
	FR 2121723	A5	19720825	FR 1972-687	19720110
	FR 2121723	B1	19730629		
				US 1971-105535	19710111
	CH 580810	A	19761015	CH 1972-308	19720110
				US 1971-105535	19710111
				US 1971-141516	19710510
	GB 1385342	A	19750226	GB 1972-1313	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510
	GB 1385343	A	19750226	GB 1974-33210	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510
	CA 1012131	A1	19770614	CA 1972-132163	19720111
				US 1971-105535	19710111
				US 1971-141516	19710510

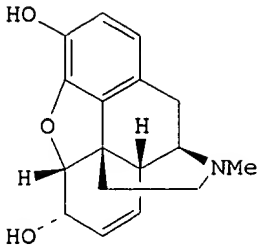
FAN 1976:538341

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3966764	A	19760629	US 1974-482200	19740624
				US 1972-270108	19720710
	US 3853914	A	19741210	US 1972-270108	19720710
				US 1971-105535	19710111
				US 1971-141516	19710510

FAN 1976:587540

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3966744	A	19760629	US 1974-482542	19740624
				US 1971-105535	19710111
				US 1971-141516	19710510
				US 1972-270108	19720710
	US 3690834	A	19720912	US 1971-141516	19710510
	FR 2121723	A5	19720825	FR 1972-687	19720110
	FR 2121723	B1	19730629		
				US 1971-105535	19710111
	US 3853914	A	19741210	US 1972-270108	19720710
				US 1971-105535	19710111
				US 1971-141516	19710510

GI



II

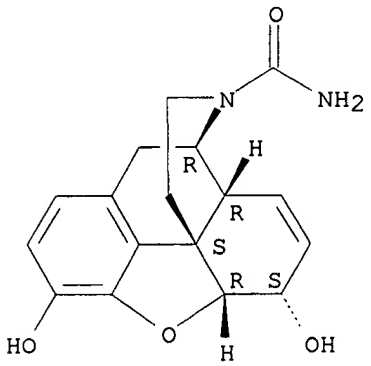
AB Spin-labeled compds. (ligand analogs) for use in immunoassay detn. of pollutants or illicit drugs (ligands) in body fluids were prepd. by modifn. of the biol. active compd. or a structural analog and coupling with a stable free radical compd. The ligand analog is recognizable by a receptor mol. (an antibody) and can compete with the ligand for the receptor site in such a way that the ligand concn. can be detd. by ESR spectroscopy. For example, 153 mg morphine (II) [57-27-2] in 4 ml abs. EtOH was treated with 146 mg 4-bromoacetamido-2,2,6,6-tetramethylpiperidino-1-oxyl [55738-74-4] under N to give 4-[2'-(O311-morphino)acetamido]-2,2,6,6-tetramethylpiperidino-1-oxyl (I) [41370-64-3], a ligand analog. Aminoethyl-Bio-Gel-P-60 (400 mg), 300 mg O3-carboxymethylmorphine [41093-72-5], and 1 g NaHCO3 were mixed in 20 ml DMF, the product was suspended in 20 ml rabbit serum contg. morphine antibodies, and the suspension was filtered. The residue was suspended in phosphate buffer (pH 3.8), the gel was sepd. and the supernatant liq. was dialyzed against phosphate buffer (pH 7.4) to give a buffered soln. of antibodies. A suspension of 50 mg p-aminobenzamidoethyl-Bio-Gel-P-60 in 10 ml H2O was acidified to pH 4.5 (HCl) and treated with 6 mg NaNO2 in 2 ml H2O. The morphine antibody soln. (1 ml, 10-5M) was added and 20 mg resorcinol was added 40 min later. The supported suspended morhpine antibodies (50 mg) were suspended in 10 ml pH 8 borate buffer contg. 10-8M concn. of I. The solid obtained showed ESR signals indicating binding of the free radical-labeled morphine analog to the receptor (antibody).

IT **56740-96-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 56740-96-6 CAPLUS

CN Morphinan-17-carboxamide, 7,8-didehydro-4,5-epoxy-3,6-dihydroxy-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 26 OF 37 CAPLUS COPYRIGHT 2001 ACS

AN 1975:572838 CAPLUS

DN 83:172838
TI Normorphine derivatives bonded to proteins
IN Schneider, Richard S.
PA Syva Co., USA
SO U.S., 9 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

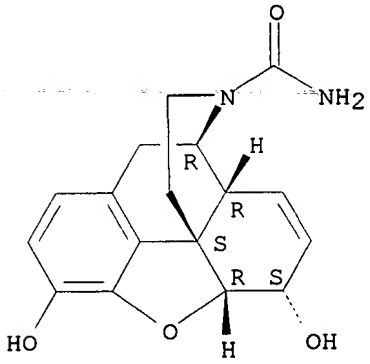
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3884898	A	19750520	US 1972-281883	19720818

GI For diagram(s), see printed CA Issue.

AB N-carboxymethylnormorphine (I) [56740-97-7], prepd. by the reaction of normorphine [466-97-7] with Na bromoacetate [1068-52-6], was capable of conjugating with proteins, and was used in an immunoassay method which detected morphine [57-27-2] in the presence of morphine metabolites or codeine. Antisera was prepd. in rabbits and the assay carried out in sheep. Spin labeled 3-[2-(N-normorphino)acetamido]-2,2,5,5-tetramethylpyrrolidine-1-oxyl [**56740-99-9**] was also prepd. and used in the immunoassay method.

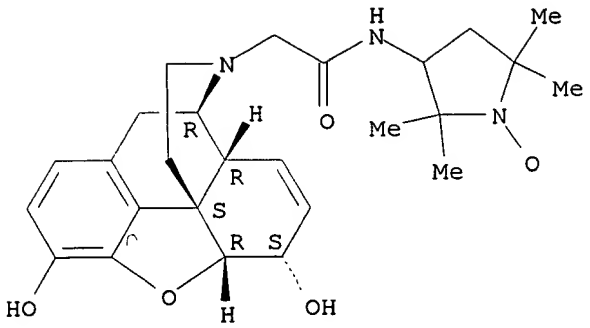
IT **56740-96-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and decarbamoylation of)
RN 56740-96-6 CAPLUS
CN Morphinan-17-carboxamide, 7,8-didehydro-4,5-epoxy-3,6-dihydroxy-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **56740-99-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and protein conjugation of, in morphine immunoassay)
RN 56740-99-9 CAPLUS
CN 1-Pyrrolidinyloxy, 3-[[[(5.alpha.,6.alpha.)-7,8-didehydro-4,5-epoxy-3,6-dihydroxymorphinan-17-yl]acetyl]amino]-2,2,5,5-tetramethyl- (9CI) (CA INDEX NAME)

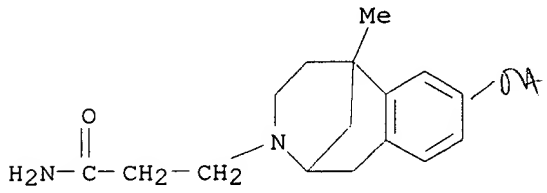
Absolute stereochemistry.



L5 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1975:43193 CAPLUS
DN 82:43193
TI Derivatives of 2-substituted-cyanoalkylbenzomorphane
IN Atsumi, Toshio; Kobayashi, Kenkji; Takebayashi, Yoshiaki; Yamamoto, Hisao
PA Sumitomo Chemical Co., Ltd.
SO Japan. Kokai, 6 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 49072261	A2	19740712	JP 1972-116023	19721118

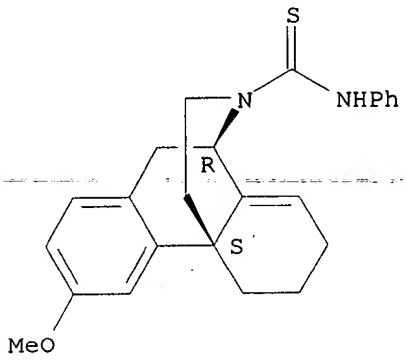
GI For diagram(s), see printed CA Issue.
AB I (R4-H, OH, lower alkoxy, alkanoyloxy, or reactive ester group; R1 = H, lower alkyl, alkoxyalkyl or aryl; R2, R3, and R4 = H, lower alkyl; R5 = reactive ester group) were treated with alkali cyanide to give I (R5 = CN), which were also prepd. by dehydration of I (R5 = CONH2). I (R5 = CN) are analgesics (no data). Thus, a mixt. of 2.5 g NaCN, 2.3 g 2'-tosyloxy-2-(.beta.-tosyloxyethyl)-5,9-dimethyl-6,7-benzomorphan and Me2SO was refluxed 8 hr. H2O added, and refluxed another 1 hr to give 0.4 g 2'-hydroxy-2-(.beta.-cyanoethyl)-5,9-dimethyl-6,7-benzomorphan. Also, a mixt. of 0.5 g 2-(.beta.-amidocarbonylethyl)-5-methyl-6,7-benzomorphan and 2.5 g POCl3 was refluxed 2 hr to give 0.2 g the corresponding 2-(.beta.-cyanoethyl)benzomorphan.
IT **54523-96-5**
RL: RCT (Reactant)
(dehydration of)
RN 54523-96-5 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-propanamide, 1,4,5,6-tetrahydro-6-methyl- (9CI) (CA INDEX NAME)



L5 ANSWER 28 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1974:520823 CAPLUS

DN 81:120823
TI Synthetic morphinans and hasubanans. II. Mechanism of acid-catalyzed transformations of 17-(N-phenylthioamido)-3-methoxy-.DELTA.8,14-morphinan
AU Saucier, Michel; Monkovic, Ivo
CS Bristol Lab. Canada, Candiac, Que., Can.
SO Can. J. Chem. (1974), 52(15), 2736-43
CODEN: CJCHAG
DT Journal
LA English
AB The acid-catalyzed rearrangement of the (phenylthioamido)morphinan I to the (phenylthioamido)-hasubanan II, and acid-catalyzed cyclization of II to the thiazinohasubanan III were described. Both transformations were discussed in terms of intramolecular vs. intermolecular hydride (proton) transfers. The redn. of III afforded 3-methoxy-10.beta.-mercaptohasubanan (IV, R = SH), which was further hydrogenolized to 3-methoxyhasubanan (IV, R = H).
IT **54313-12-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and acid catalyzed rearrangement of)
RN 54313-12-1 CAPLUS
CN Morphinan-17-carbothioamide, 8,14-didehydro-3-methoxy-N-phenyl- (9CI) (CA INDEX NAME)

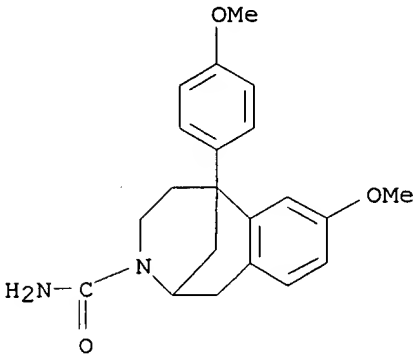
Absolute stereochemistry.



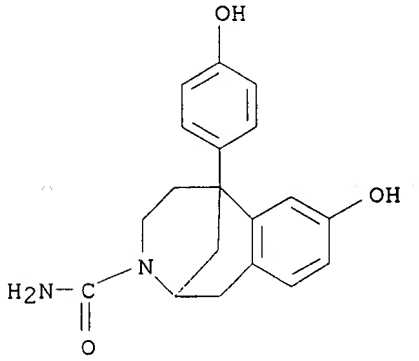
L5 ANSWER 29 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1974:37022 CAPLUS
DN 80:37022
TI Analgesic 6,7-benzomorphans
IN Atsumi, Toshio; Kobayashi, Kenji; Takebayashi, Yoshiaki; Yamamoto, Hisao
PA Sumitomo Chemical Co., Ltd.
SO Ger. Offen., 16 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2323148	A1	19731122	DE 1973-2323148	19730508
				JP 1972-45683	19720508
	JP 49001567	A2	19740108	JP 1972-45683	19720508
	CA 978943	A1	19751202	CA 1973-169638	19730426
				JP 1972-45683	19720508
	GB 1415733	A	19751126	GB 1973-20430	19730430
				JP 1972-45683	19720508
	FR 2183762	A1	19731221	FR 1973-15915	19730503
	FR 2183762	B1	19780324		

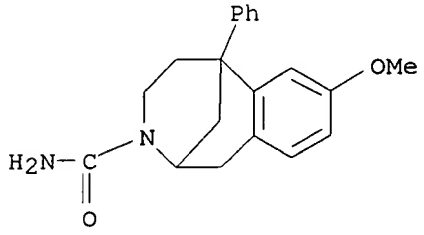
RN 5099-40-1 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide,
1,4,5,6-tetrahydro-8-methoxy-
6-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



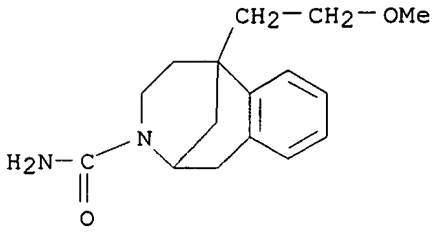
RN 5099-77-4 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide,
1,4,5,6-tetrahydro-8-hydroxy-
6-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)



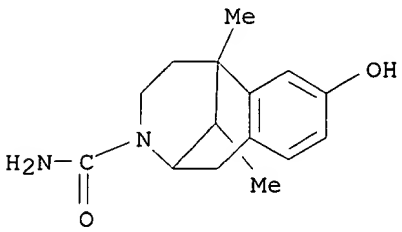
RN 5195-98-2 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide,
1,4,5,6-tetrahydro-8-methoxy-
6-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



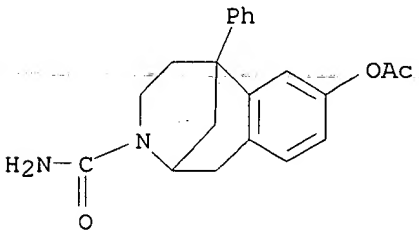
RN 18136-36-2 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide, 1,4,5,6-tetrahydro-6-(2-
methoxyethyl)- (8CI, 9CI) (CA INDEX NAME)



RN 42753-42-4 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide, 1,4,5,6-tetrahydro-8-hydroxy-6,11-dimethyl- (9CI) (CA INDEX NAME)



RN 42753-44-6 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide, 8-(acetyloxy)-1,4,5,6-tetrahydro-6-phenyl- (9CI) (CA INDEX NAME)



L5 ANSWER 31 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1972:59477 CAPLUS
DN 76:59477
TI 3-Carbamoyl-1,2,3,4,5,6-hexahydro-2,6-methano-3-benzazocines
IN Haberli, Jorg
PA Geigy Chemical Corp.
SO U.S., 3 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3625948	A	19711207	US 1968-738853	19680621

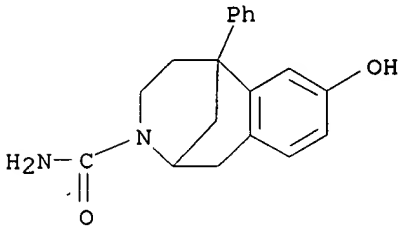
GI For diagram(s), see printed CA Issue.
AB Five title compds. (I, R=H, OH, or OMe; R1=Ph, MeOCH2CH2, 3,4-Me2C6H3, or p-ClC6H4; R2=CONH2) were easily prepd. in .gtoreq.90% yields by treating the 3-unsubstituted I with urea. Thus, I (R=Ph, R1=AcO, and R2=Me) in toluene and aq. ClCO2Et was heated to give I (R=Ph, R1=AcO and R2=CO2Et), which was mixed in Et Carbitol with KOH to give I (R=Ph, R1=OH, and R2=H), which was then heated with aq. urea, HCl, and HOAc soln. to give the title

I (R=Ph, R1=OH, and R2=CONH2).

IT **5099-78-5P 5251-10-5P 18136-36-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

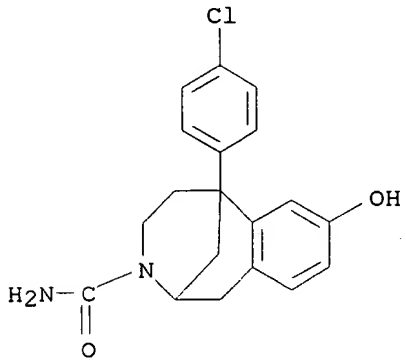
RN 5099-78-5 CAPLUS

CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide, 1,4,5,6-tetrahydro-8-hydroxy-6-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



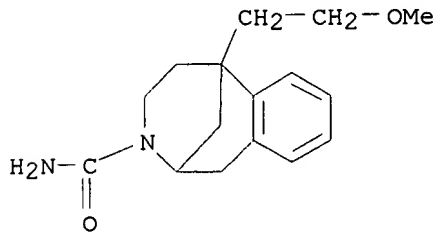
RN 5251-10-5 CAPLUS

CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide, 6-(4-chlorophenyl)-1,4,5,6-tetrahydro-8-hydroxy- (9CI) (CA INDEX NAME)



RN 18136-36-2 CAPLUS

CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide, 1,4,5,6-tetrahydro-6-(2-methoxyethyl)- (8CI, 9CI) (CA INDEX NAME)



L5 ANSWER 32 OF 37 CAPLUS COPYRIGHT 2001 ACS

AN 1971:111932 CAPLUS

DN 74:111932

TI 3-Cyano-1,2,3,4,5,6-hexahydro-2,6-methano-3-benzazocines

IN Clarke, Frank Henderson, Jr.; Block, Fred B.

PA Geigy Chemical Corp.

SO U.S., 7 pp. Continuation-in-part of U.S. 3341538
CODEN: USXXAM

DT Patent

LA English
FAN.CNT 1

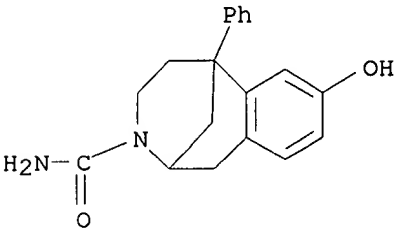
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 3558638	A	19710126	US 1968-764968	19681003

AB 3-Methyl-2,6-methano-3-benzazocines, prepd. according to the previous patent, are treated with BrCN to give the corresponding 3-cyano compds., useful as nontoxic analgesics. Typical compds. include 8-acetoxy-3-cyano-1, 2,3,4,5,6 - hexahydro - 6-phenyl-2,6-methano-3-benzazocine and 3-cyano-1,2,3,4,5,6-hexahydro-8-methoxy-6-phenyl-2,6-methano-3-benzazocine.

IT **5099-78-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 5099-78-5 CAPLUS

CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide, 1,4,5,6-tetrahydro-8-hydroxy-6-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



L5 ANSWER 33 OF 37 CAPLUS COPYRIGHT 2001 ACS

AN 1970:520797 CAPLUS

DN 73:120797

TI Derivatives of morphinan

IN Leimgruber, Willy; Mohacsi, Ernest

PA Hoffmann-La Roche, F., und O., A.-G.

SO Fr., 17 pp.
CODEN: FRXXAK

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI FR 1584396		19691219		
			US	19670825

GI For diagram(s), see printed CA Issue.

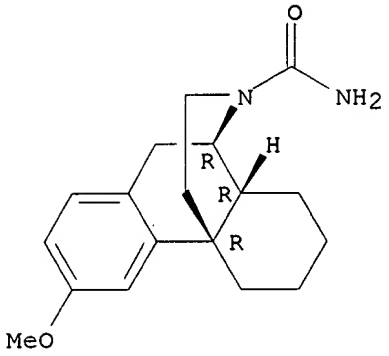
AB Title products with pharmacol. activity, are prepd. A soln. of (.+-.)-1-(p-methoxybenzyl)-1,2,3,4,5,6,7,8-octahydroisoquinoline (I) in HCO2Me is refluxed 27 hr to give (.+-.)-1-(p-methoxybenzyl)-2-formyl-1,2,3,4,5,6,7,8-octahydroisoquinoline (II), m. 59-61.degree.. H3PO4 (99.3%) and II is heated 24 hr at 70.degree. to give (.+-.)-3-methoxy-N-formylmorphinan (III). A mixt. of III and LiAlH4 in anhyd. THF is refluxed 2 hr to give (.+-.)-3-methoxy-N-methylmorphinan (IV), m. 82-4.degree.. A soln. of III in aq. 2.5N NaOH is refluxed 16 hr to give (.+-.)-3-methoxymorphinan (V), b0.05 140-5.degree.. A soln. of V, aq. 37%
HCHO, and Raney Ni in MeOH is hydrogenated 8 hr at room temp. to give IV. Four other morphinans are similarly prepd.

IT **28973-52-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 28973-52-6 CAPLUS

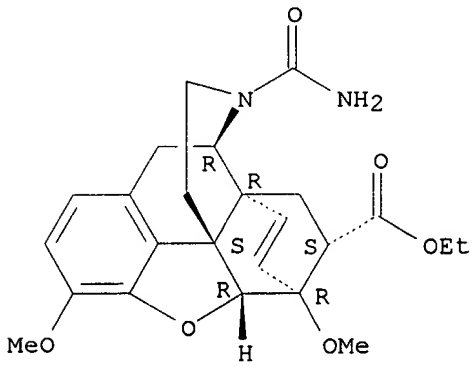
CN Morphinan-17-carboxamide, 3-methoxy-, (.+-.)- (8CI) (CA INDEX NAME)

Relative stereochemistry.



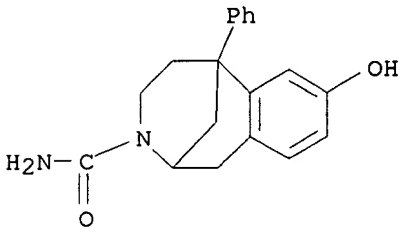
L5 ANSWER 34 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1970:3611 CAPLUS
DN 72:3611
TI Novel analgesics and molecular rearrangements in the morphine-thebaine group. XIII. 7-Aminomethyl-6,14-endo-ethenotetrahydrothebaines
AU Bentley, Kenneth W.; Bower, J. D.; Lewis, John William; Readhead, M. J.; Smith, Alan Charles Brandon; Young, G. R.
CS Res. Lab., Reckitt and Sons Ltd., Kingston upon Hull, Engl.
SO J. Chem. Soc. C (1969), (17), 2237-40
CODEN: JSOOAX
DT Journal
LA English
GI For diagram(s), see printed CA Issue.
AB A series of 7-aminomethyl-6,14-endo-ethenotetrahydrothebaine (I) was prepd. from the corresponding 7-ethoxycarbonyl and 7-carbamoyl compds.
IT **24485-15-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 24485-15-2 CAPLUS
CN 6,14-Ethenomorphinan-7-carboxylic acid, 17-(aminocarbonyl)-4,5-epoxy-3,6-dimethoxy-, ethyl ester, (5.alpha.,7.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

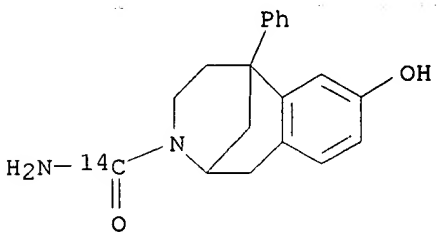


L5 ANSWER 35 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1969:524196 CAPLUS
DN 71:124196
TI 1,2,3,4,5,6-Hexahydro-6-phenyl-2,6-methano-3-benzazocines. I. 3-Carboxamido-8-hydroxy derivative as an orally effective analgetic
AU Block, Fred B.; Clarke, Frank Henderson, Jr.
CS Pharm. Div., Geigy Chem. Corp., Ardsley, N. Y., USA

SO J. Med. Chem. (1969), 12(5), 845-7
CODEN: JMCMAR
DT Journal
LA English
GI For diagram(s), see printed CA Issue.
AB The synthesis of 3-carbamoyl-1,2,3,4,5,6-hexahydro-2,6-methano-3-benzazocin-8-ol (I) is described. In a preliminary clinical trial I has been shown to be an orally effective analgetic. This compd. has an unusual freedom from toxicity in rats and dogs, and from physical dependence capacity in the monkey.
IT **5099-78-5P 24119-20-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 5099-78-5 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide,
1,4,5,6-tetrahydro-8-hydroxy-
6-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 24119-20-8 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide-carbonyl-14C,
1,4,5,6-tetrahydro-8-hydroxy-6-phenyl- (8CI) (CA INDEX NAME)



L5 ANSWER 36 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1968:105016 CAPLUS
DN 68:105016
TI 2,6-Methano-3-benzazocines
IN Block, Fred B.; Clarke, Frank Henderson, Jr.
PA Geigy Chemical Corp.
SO U.S., 15 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 3341538		19670912	US	19650618

GI For diagram(s), see printed CA Issue.
AB Title compds. (I) were prepd. Thus, a soln. of 0.675 mole redistd. 1-methyl-4-piperidone was added with stirring to an ice cold C6H6-Et2O soln. contg. 0.74 mole PhLi during 45 min. After the reaction mixt. reached room temp. while stirring (2 hrs.), it was worked up to give oily 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine, b0.9 103-14.degree..

p-Methoxybenzyl chloride (0.58 mole) in 50 cc. Me2CO was added dropwise to a stirred soln. of 0.45 mole of the above compd. in 350 cc. Me2CO at reflux, and the mixt. after stirring at reflux 2 hrs., was worked up to give 1-methyl-1-(4-methoxybenzyl)-4-phenyl-1,2,5,6-tetrahydropyridinium chloride, m. 119-26.degree., 123-6.degree., and 167-70.degree. for three separate prepns. A suspension of 1.05 mole of this quaternary salt in Et2O was treated with 0.98 mole BuLi in Et2O (1.56 N) under N with stirring, over 1 hr. and worked up to give 1-methyl-2-(4-methoxybenzyl)-4-phenyl-1,2,5,6-terrahydropyridine (II), b2 135-225.degree.. II.HBr (IIa) m. 170-2.degree.; II.HCl (IIb) m. 119-24.degree.. A soln. of 32.7 g. IIa in 330 cc. 48% HBr was refluxed 4.5 hrs. and worked up to give 1,2,3,4,5,6-hexahydro-3-methyl-6-phenyl-2,6-methano-3-benzazocin-8-ol (III), m. 249-52.degree. (MeOH). III (1.68 g.) was treated with 8.4 cc. Ac2O at 100.degree. for 45 min. to give 8-acetoxy-1,2,3,4,5,6-hexahydro-3-methyl-6-phenyl-2,6-methano-3-benzazocine (IV), m. 112-20.degree. [(iso-Pr)2O]. IV.HCl.H2O partially m. 180-90.degree., clear at 250-3.degree.. A soln. of 6.5 g. IV in 30 cc. CHCl3 was added to a soln. of 2.6 g. BrCN in 30 cc. CHCl3 during 45 min., and the mixt. refluxed 3 hrs. and worked up to yield 8-acetoxy-3-cyano-1,2,3,4,5,6-hexahydro-6-phenyl-2,6-methano-3-benzazocine (V), m. 207-9.degree. (EtOH). To a mixt. of 9.0 g. V, 9.7 cc. 30% H2O2, and 30 cc. EtOH, 5.6 cc. 6N NaOH was added slowly with stirring at 35-40.degree., and the mixt. stirred 3.5 hrs. at 50-60.degree. and worked up to yield 3-carbamoyl-1,2,3,4,5,6-hexahydro-6-phenyl-2,6-methano-3-benzazocin-8-ol (VI), m. 292-4.degree. (MeOH), also prepd. from 1.92 g. IV in 30 cc. CHCl3 and 0.76 g. BrCN in 15 cc. CHCl3 followed by hydrolysis with 25 cc. 6% aq. HCl. A soln. of 1.59 g. IV in 50 cc. dry C6H6 was added to a soln. of 1.5 g. ClCO2Et in 25 cc. dry C6H6 during 45 min. After refluxing 2 hrs. and stirring 15 hrs., the soln. was worked up to yield 8-acetoxy-3-carbethoxy-1,2,3,4,5,6-hexahydro-6-phenyl-2,6-methano-3-benzazocine. A mixt. of 0.8 g., this compd. and 40 cc. 2N HCl was refluxed 17 hrs. and worked up to give 3-carbethoxy-1,2,3,4,5,6-hexahydro-6-phenyl-2,6-methano-3-benzazocin-8-ol, m. 207-8.degree. (C6H6-petroleum ether). Similarly, 3.21 g. IV was treated with 1.7 g. ClCO2Ph in 35 cc. dry C6H6 to give 8-acetoxy-3-carbophenoxy-1,2,3,4,5,6-hexahydro-6-phenyl-2,6-methano-3-benzazocine (VII). A mixt. of 5.0 g. VII and 25 g. dry NHMe2 was heated at 50.degree. 12 hrs. (sealed tube) and worked up to yield 3-(N,N-dimethylcarbamoyl)-1,2,3,4,5,6-hexahydro-6-phenyl-2,6-methano-3-benzazocin-8-ol. 3-(N-Piperidinylcarbonyl)-1,2,3,4,5,6-hexahydro-6-phenyl-2,6-methano-3-benzazocin-8-ol was also prepd. by refluxing 5 g. VII and 25 cc. dry piperidine 12 hrs. 3-(N-Morpholinocarbonyl)-1,2,3,4,5,6-hexahydro-6-phenyl-2,6-methano-3-benzazocin-8-ol was similarly prepd. To a suspension of 5.60 g. LiAlH4 in 100 cc. dry tetrahydrofuran (THF), 5.0 g. V in 100 cc. dry THF was added with heating, and the mixt. refluxed 17 hrs. and worked up to give 1,2,3,4,5,6-hexahydro-6-phenyl-2,6-methano-3-benzazocin-8-ol (VIII), m. 239-41.degree. (iso-PrOH). A mixt. of 5 g. VIII and 5 g. NH4CNS was heated to give a clear melt, which gave (EtOH), 1,2,3,4,5,6-hexahydro-6-phenyl-3-thiocarbamyl-2,6-methano-3-benzazocin-8-ol. also prepd. from V in 50 cc. pyridine satd. with H2S. A soln. of 1.0 g. VIII and 0.3 g. MeSCN in 70 cc. dry THF was refluxed 18 hrs. to give 1,2,3,4,5,6-hexahydro-3-(N-methylthiocarbamyl)-6-phenyl-2,6-methano-3-benzazocin-8-ol (IX), m. 263-6.degree. (1:2 AcOEt-cyclohexane), m. 265-7.degree. (50% aq. MeOH). A soln. of 1.20 g. VIII and 0.82 g. .beta.-phenethyl isothiocyanate in 80 cc. dry THF was refluxed 3 hrs. to give 1,2,3,4,5,6-hexahydro-6-phenyl-3-[N-(.beta.-phenethyl)thiocarbamoyl]-2,6-methano-3-benzazocin-8-ol (X), m.

234-6.degree.. A soln. of 1.0 g. VIII and 0.42 g. allyl isothiocyanate in 65 cc. dry THF was refluxed 18 hrs. to give 3-(N-allylthiocarbamoyl)-1,2,3,4,5,6-hexahydro-6-phenyl-2,6-methano-3-benzazocin-8-ol (XI), m. 183-9.degree., m. 199-201.degree. (AcOEt). A mixt. of 5.0 g. IX, 25.0 g. HgO, and 100 cc. abs. EtOH was stirred at reflux 24 hrs. to give 1,2,3,4,5,6-hexahydro-3-(N-methylcarbamoyl)-6-phenyl-2,6-methano-3-benzazocin-8-ol. A soln. of 2.25 g. Na in 25 cc. abs. MeOH was added to a soln. of 17.2 g. PhMe3NCl in 25 cc. abs. MeOH. After filtration, 25.0 g. III in PhMe was added to the filtrate. The mixt. was heated with stirring to remove the solvents (100-10.degree.) and worked up to give 1,2,3,4,5,6-hexahydro-8-methoxy-3-methyl-6-phenyl-2,6-methano-3-benzazocine, also prepd. from 8.0 g. IIb and 24 g. AlBr3 in 150 cc. CS2. A soln. of 6.5 g. of the above compd. in 100 cc. CHCl3 was added to a soln. of 2.6 g. BrCN in 30 cc. CHCl3 during 45 min., and refluxed 3 hrs. to give 3-cyano-1,2,3,4,5,6-hexahydro-8-methoxy-6-phenyl-2,6-methano-3-benzazocine (XII). XII (5.0 g.) in 100 cc. dry THF was added to a suspension of 5.6 g. LiAlH4 in 100 cc. dry THF, and the mixt. refluxed 17 hrs. and worked up to give 1,2,3,4,5,6-hexahydro-8-methoxy-6-phenyl-2,6-methano-3-benzazocine. A soln. of 6.0 g. PhSCN in 20 cc. C6H6 was slowly added to a stirred soln. of the above compd. in 100 cc. C6H6, and the mixt. refluxed 1 hr. to give 1,2,3,4,5,6-hexahydro-8-methoxy-3-(N-phenylcarbamoyl)-6-phenyl-2,6-methano-3-benzazocine. A mixt. of 3.0 g. 4-(p-chlorophenyl)-1,2,5,6-tetrahydropyridine-HCl, 2.36 g. AcONa, 7.9 cc. 37% HCHO and 3.62 g. 91% HCO2H was heated with stirring 2 hrs. at 95.degree. and worked up to give 1-methyl-4-(p-chlorophenyl)-1,2,5,6-tetrahydropyridine, m. 90-1.degree.. This compd. (9.66 g.) was refluxed with 9.12 g. p-methoxybenzyl chloride in 10 cc. Me2CO 1 hr. to give 1-methyl-1-(p-methoxybenzyl)-4-(p-chlorophenyl)-1,2,5,6-tetrahydropyridinium chloride, m. 194.0-5.5.degree.. PhLi (5.50 cc., 2N) was added to 3.30 g. of the above dried compd. slurried in 50 cc. dry Et2O under N and the mixt. refluxed 2 hrs. and worked up to give

1-methyl-2-(p-methoxybenzyl)-4-(p-chloropheny)-1,2,5,6-tetrahydropyridine-HBr, m. 181-2.degree.. A mixt. of this compd. (8.72 g.) and 131 cc. 48% HBr was refluxed with stirring 19 hrs. and worked up to give

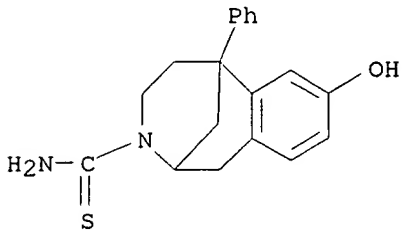
6-(p-chlorophenyl)-1,2,3,4,5,6-hexahydro-3-methyl-2,6-methano-3-benzazocin-8-ol, m. 272-4.degree.. This compd. (1.02 g.) was treated with 7.0 cc. Ac2O at 100.degree. 1 hr. to give 8-acetoxy-6-(p-chlorophenyl)-1,2,3,4,5,6-hexahydro-3-methyl-2,6-methano-3-benzazocine, m. 115-17.degree. (iso-PrOH petroleum ether). A soln. of 3.0 g. of this compd. in 80 cc. CHCl3 was added to a soln. of 1.07 g. BrCN in 40 cc. CHCl3 during 1 hr., and the soln. refluxed 3 hrs. and worked up to give 8-acetoxy-3-cyano-6-(p-chlorophenyl)-1,2,3,4,5,6-hexahydro-2,6-methano-3-benzazocine, m. 168-70.degree.. A mixt. of 2.40 g. of this compd., 2.34 cc. 30% H2O2, and 40 cc. EtOH was stirred while 1.36 cc. 6N NaOH was added slowly at room temp. After the temp. rose 15.degree., the soln. was heated 3 hrs. at 55.degree. and worked up to give 3-carbamoyl-6-(p-chlorophenyl)-1,2,3,4,5,6-hexahydro-2,6-methano-3-benzazocin-8-ol, m. 170-7.degree.. MeI (313 g.) was added dropwise with stirring to a soln. of 274 g. 4-(.beta.-methoxyethyl)pyridine in 400 cc. Me2CO and 200 cc. C6H6 so as to maintain reflux and the mixt. stirred, and allowed to cool to room temp. during 3 hrs. and refrigerated overnight to give 4-(.beta.-methoxyethyl)pyridine methiodide, m. 74-8.degree.. A soln. of 223 g. of this compd. in 640 cc. 50% MeOH was added dropwise with stirring to a soln. of 1.3 mole NaBH4 in 240 cc. H2O at a rate to maintain the temp. at 50-60.degree. (2 hrs.). Addnl. NaBH4 (44 g.) was then added stirring at room temp. continued 15 hrs., and the soln. worked up to give

1-methyl-4-(.beta.-methoxyethyl)-1,2,5,6-tetrahydropyridine, b12 90-2.degree.. A 10% mole excess of PhCH2Cl was added to a soln. of 7.8 g. of the above compd. in 30 cc. Me2CO. After standing at room temp., the product crystd. to yield 1-benzyl-1-methyl-4-(.beta.-methoxyethyl)-1,2,5,6-tetrahydropyridinium chloride, m. 134.5-7.5.degree. (Me2CO). This compd. was very hygroscopic. A 2M soln. of PhLi in Et2O (72.5 cc., 0.143 mole) was added dropwise to a stirred suspension of the above dry compd. (0.127 mole) in 225 cc. dry Et2O at a rate to maintain gentle reflux. After refluxing 2 hrs., the mixt. was worked up to give 2-benzyl-4-(.beta.-methoxyethyl)-1-methyl-1,2,5,6-tetrahydropyridine, b0.5 128-35.degree.. A soln. of the sol. portion of 12.0 g. AlBr3 in 20 cc. CS2 was added during 10 min. to a soln. of 3.0 g. of the above compd. in 20 cc. CS2 with stirring and cooling in ice. After 5 min., the mixt. was refluxed 30 min. and worked up to give 1,2,3,4,5,6-hexahydro-6-(.beta.-methoxyethyl)-3-methyl-2,6-methano-3-benzazocine (XIII), b0.05 130.degree.; HCl salt m. 163-5.degree. (Me2CO). A soln. of 5 cc. ClCO2Et in 35 cc. PhMe was added with stirring under N to a soln. of 10.35 g. XIII in 35 cc. PhMe. The soln. was refluxed 6 hrs. and worked up to give 3-carbethoxy-1,2,3,4,5,6-hexahydro-6-(.beta.-methoxyethyl)-2,6-methano-3-benzazocine. To a soln. of 0.022 mole of the above compd. in 20 cc. glacial AcOH chilled to -10.degree., was added a mixt. of 20 cc. fuming HNO3 (90%) and 15 cc. glacial AcOH at -10 to <+5.degree., and the mixt. kept at room temp. 63 hrs. and worked up to yield a picrate, m. 212.5.degree., which with excess 5% LiOH gave a light tan oil. This oil (1.96 g.) was dissolved in a mixt. of 80 cc. 95% EtOH and 10 cc. N2H4.H2O. To this soln., a small amt. of Raney Ni was added and the mixt. heated 30 min. at 95.degree.. After filtering and concg. the filtrate, the residue was dissolved in 50 cc. 3N H2SO4, the soln. cooled to 0.degree., 0.5 g. NaNO2 added gradually, the temp. kept 30 min. at 0.degree., and the mixt. worked up to give 1,2,3,4,5,6-hexahydro-6-(.beta.methoxyethyl)-3-methyl-2,6-methano-3-benzazocin-8-ol, m. 155-9.degree. (decompn.) (PhMe-petroleum ether). Similarly, 3-carbamoyl-1,2,3,4,5,6-hexahydro-6-(.beta.-methoxyethyl)2,6-methano-3-benzazocine, m. 141-2.degree., was prepd. from XIII. .beta.-3-Carbamoyl-11-ethyl-1,2,3,4,5,6-hexahydro-6-methyl-2,6-methano-3-benzazocin-8-ol and 3-carbamyl-1,2,3,4,5,6-hexahydro-6-isopropyl-2,6-methano-3-benzazocin-8-ol were similarly prepd. MeI (15 cc.) was added to a soln. of 0.20 mole 4-isopropylpyridine in 50 cc. Me2CO. The reaction was exothermic and the methiodide crystd. in 1 hr. The mixt. was stirred for a total of 2 hrs. and worked up to give 4-isopropylpyridine methiodide, m. 123-30.degree.. This compd. must be stored under N in a brown bottle. p-MeOC6H4CH2MgCl was prepd. from 0.211 mole p-MeOC6H4CH2Cl and 0.5 mole each of Mg powder and Mg turning in 225 cc. dry Et2O. This soln., filtered through glass wool, was added to a suspension of 44.1 g. 4-isopropylpyridine methiodide in 150 cc. Et2O. After 2 hrs. reflux, the mixt. was worked up to give crude 1-methyl-2-(p-methoxybenzyl)-4-isopropyl-1,2-dihydropyridine. This in 110 cc. MeOH and 50 cc. N NaOH was added to a soln. of 21 cc. N NaOH and 0.125 mole NaBH4, and the mixt. kept 1 hr., at 65 .+-. 5.degree. and worked up to give 4-isopropyl-1-methyl-2-(p-methoxybenzyl)-1,2,5,6-tetrahydropyridine, b0.6 101-2.degree.. A mixt. of 0.0382 mole of this compd. and 100 cc. 48% HBr was heated 24 hrs. at 150.degree. and worked up to give 1,2,3,4,5,6-hexahydro-6-isopropyl-3-methyl-2,6-methano-3-benzazocin-8-ol, m. 240-2.5.degree.. A molar equiv. of 1,3-dimethyl-4-phenyl-1,2,5,6-tetrahydropyridine was converted into cis-8-acetoxy-3,11-dimethyl-1,2,3,4,5,6-hexahydro-2,6-methano-3-benzazocine by treatment in suspension with PhLi, p-methoxybenzyl chloride, BuLi, 48% HBr, and Ac2O successively as described. The cis

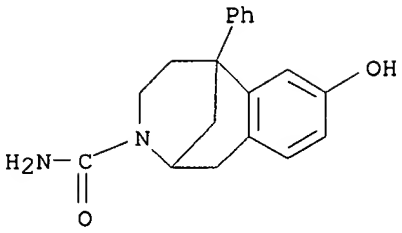
isomer was sepd. from a smaller amt. of trans isomer by fractional crystn.
of the HCl salts from MeOH-Me2CO. The trans isomer was prepd. by cyclizing the HCl salt of 1,3-dimethyl-2-(p-methoxybenzyl)-4-phenyl-1,2,5,6-tetrahydropyridine with AlBr3 as described above to yield 3,11-dimethyl-1,2,3,4,5,6-hexahydro-8-methoxy-6-phenyl-2,6-methano-3-benzazocine (XIV) which was demethylated and acetylated as described above. The cis and trans forms of 3-carbamoyl-1,2,3,4,5,6-hexahydro-11-methyl-6-phenyl-2,6-methano-3-benzazocin-8-ol were obtained from the cis and trans forms of XIV by treatment with BrCN in CHCl3 followed by hydrolysis with 6% HCl as described above. VI (3.96 g.) and 4.4 g. (+)-camphorsulfonic acid were suspended in boiling Me2CO and enough MeOH added to give a clear soln. After cooling, the salt was filtered off, dried, and recrystd. from MeOH-Me2CO to give the isomer m. 241-7.degree., [.alpha.]25D 170.degree. (c 0.5, MeOH). The salt treated with 10% aq. NH4OH, and the ppt. filtered off and dried to yield the (+)-base, m. 254-9.degree., [.alpha.]25D 173.degree. (c 0.52, MeOH). The (-)-base was recovered from the mother liquors as the (+)-tartrate. Each isomer was acetylated. VI (2.08 g.) was treated with 0.78 g. succinic anhydride and 20 cc. pyridine 1 hr. at 100.degree. and worked up to yield the hemisuccinate. The hemiphthalate was similarly prepd. from 1.0 g. phthalic anhydride and 2.0 g. VI. VI (2.0 g. was heated 20 min. with 10 cc. concd. H2SO4 and worked up to give 3-carbamyl-1,2,3,4,5,6-hexahydro-6-phenyl-2,6-methano-3-benzazocin-8-ol-sulfonic acid. VI (2 g.) was treated with 2 g. nicotinoyl chloride hydrochloride and 15 cc. pyridine 2 hrs. at 70 .+-. 10.degree. and worked up to give 3-carbamyl-1,2,3,4,5,6-hexahydro-8-(3-nicotinoyloxy)-6-phenyl-2,6-methano-3-benzozacine; the HCl salt was also prepd.

IT **5099-76-3P 5099-78-5P 5099-79-6P 5099-80-9P 5251-10-5P 5571-13-1P 18136-14-6P 18136-21-5P 18136-22-6P 18136-36-2P 18140-45-9P 18181-09-4P 18947-95-0P 18947-96-1P 18948-24-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

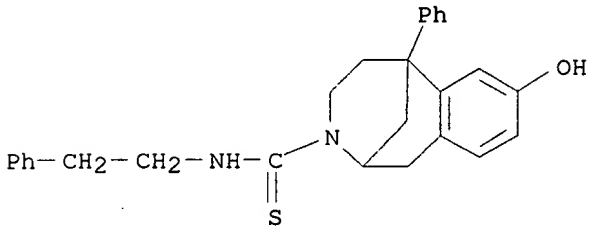
RN 5099-76-3 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide, 1,4,5,6-tetrahydro-8-hydroxy-6-phenylthio- (7CI, 8CI) (CA INDEX NAME)



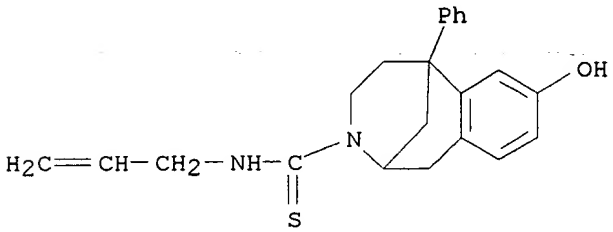
RN 5099-78-5 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide, 1,4,5,6-tetrahydro-8-hydroxy-6-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



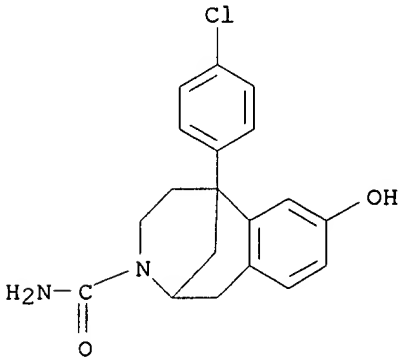
RN 5099-79-6 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide,
1,4,5,6-tetrahydro-8-hydroxy-
N-phenethyl-6-phenylthio- (7CI, 8CI) (CA INDEX NAME)



RN 5099-80-9 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide,
N-allyl-1,4,5,6-tetrahydro-8-
hydroxy-6-phenylthio- (7CI, 8CI) (CA INDEX NAME)

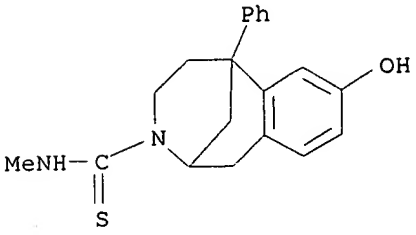


RN 5251-10-5 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide, 6-(4-chlorophenyl)-1,4,5,6-
tetrahydro-8-hydroxy- (9CI) (CA INDEX NAME)

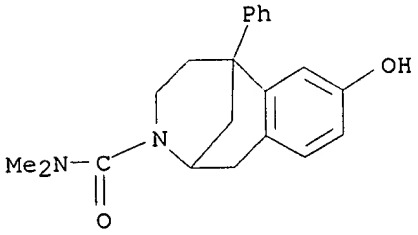


RN 5571-13-1 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide,
1,4,5,6-tetrahydro-8-hydroxy-

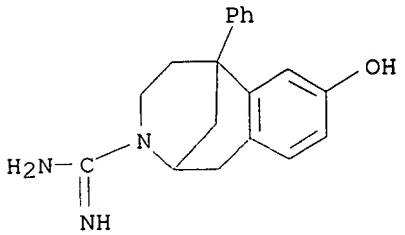
N-methyl-6-phenylthio- (8CI) (CA INDEX NAME)



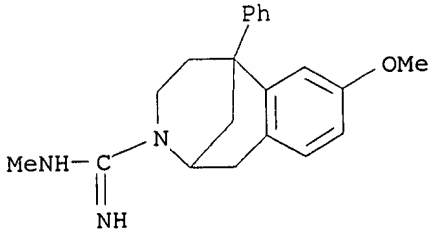
RN 18136-14-6 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide, 1,4,5,6-tetrahydro-8-hydroxy-N,N-dimethyl-6-phenyl- (8CI) (CA INDEX NAME)



RN 18136-21-5 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamidine, 1,4,5,6-tetrahydro-8-hydroxy-6-phenyl- (8CI) (CA INDEX NAME)



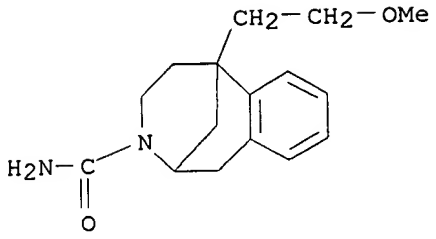
RN 18136-22-6 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamidine, 1,4,5,6-tetrahydro-8-methoxy-N-methyl-6-phenyl-, monohydrochloride (8CI) (CA INDEX NAME)



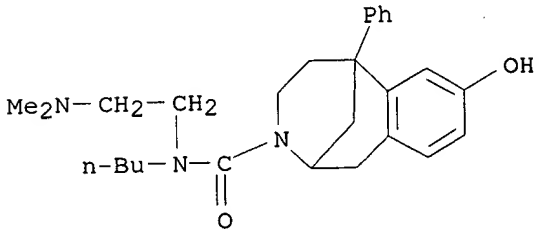
HCl

RN 18136-36-2 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide, 1,4,5,6-tetrahydro-6-(2-

methoxyethyl)- (8CI, 9CI) (CA INDEX NAME)



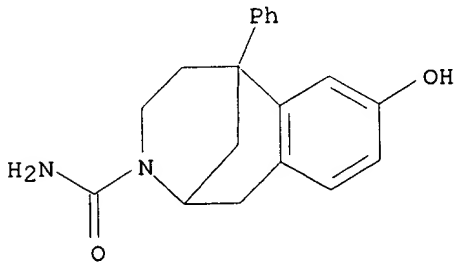
RN 18140-45-9 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide, N-butyl-N-[2-(dimethylamino)ethyl]-1,4,5,6-tetrahydro-8-hydroxy-6-phenyl-, monohydrobromide (8CI) (CA INDEX NAME)



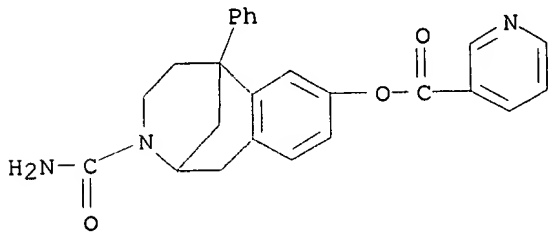
● HBr

RN 18181-09-4 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide, 1,4,5,6-tetrahydro-8-hydroxy-6-phenyl-, (+)- (8CI) (CA INDEX NAME)

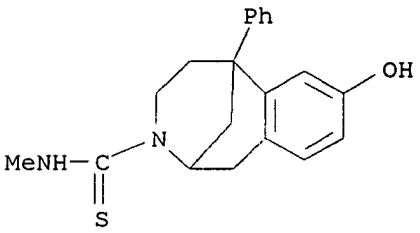
Rotation (+).



RN 18947-95-0 CAPLUS
CN Nicotinic acid, ester with 1,4,5,6-tetrahydro-8-hydroxy-6-phenyl-2,6-methano-3-benzazocine-3(2H)-carboxamide (8CI) (CA INDEX NAME)

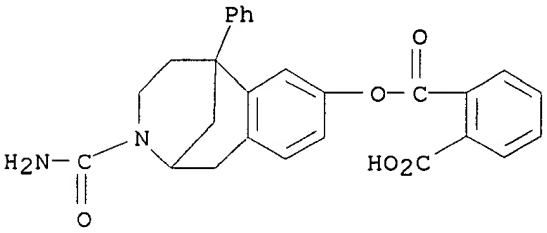


RN 18947-96-1 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-carboxamide,
1,4,5,6-tetrahydro-8-hydroxy-
N-methyl-6-phenylthio-, monohydriodide (8CI) (CA INDEX NAME)



● HI

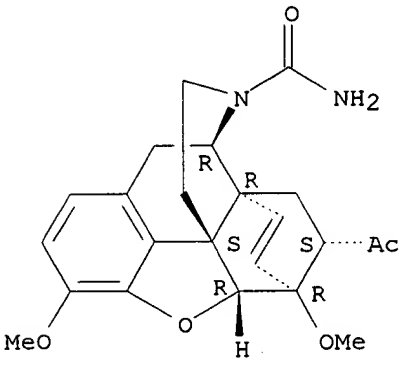
RN 18948-24-8 CAPLUS
CN Phthalic acid, monoester with 1,4,5,6-tetrahydro-8-hydroxy-6-phenyl-2,6-methano-3-benzazocine-3(2H)-carboxamide (8CI) (CA INDEX NAME)



L5 ANSWER 37 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1967:464586 CAPLUS
DN 67:64586
TI Novel analgesics and molecular rearrangements in the morphine-thebaine group. III. Alcohols of the 6,14-endo-ethenotetrahydrooripavine series and derived analogs of N-allylnormorphine and -norcodeine
AU Bentley, Kenneth W.; Hardy, Denis G.
CS Reckitt Sons Ltd., Kingston-upon-Hull, Engl.
SO J. Am. Chem. Soc. (1967), 89(13), 3281-92
CODEN: JACSAT
DT Journal
LA English
GI For diagram(s), see printed CA Issue.
AB cf. CA 67: 43960p. Secondary and tertiary alcs. of general structures I and II were prepd. by the demethylation of the corresponding bases III and IV (loc. cit.). The phenols so obtained are analgesics of extremely high potency, up to an unprecedented 12,000 times that of morphine. The bases of this and earlier series were converted into analogs of N-allylnormorphine and N-allylnorcodeine (V) via the N-cyanonor compds. and via novel N,N'-methylenebis compds. resulting from the reaction of III and IV with methyl azodicarboxylate. Some bases of the V series are morphine antagonists of unprecedented potency, up to 150 times that of N-allylnormorphine. 15 references.
IT **16524-37-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 16524-37-1 CAPLUS
CN 6,14-endo-Ethenotetrahydrothebaine, 7.alpha.-acetyl-17-carbamoyl-17-demethyl- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



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=> s e3-e4

             1 142740-96-3/RN
             1 142740-97-4/RN
L1           2 (142740-96-3/RN OR 142740-97-4/RN)

=> d 1-2


L1   ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2001 ACS
RN   142740-97-4  REGISTRY
CN   Guanidine, [(5.alpha.,6.alpha.)-3-[3,6-bis[[(1,1-
     dimethylethyl)dimethylsilyl]oxy]-4,5-epoxymorphinan-17-yl]propyl]-,
     sulfate (1:1) (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Morphinan, guanidine deriv.
MF   C32 H56 N4 O3 Si2 . H2 O4 S
SR   CA
LC   STN Files:   CA, CAPLUS, TOXLIT

     CM   1

     CRN  142740-96-3
     CMF  C32 H56 N4 O3 Si2
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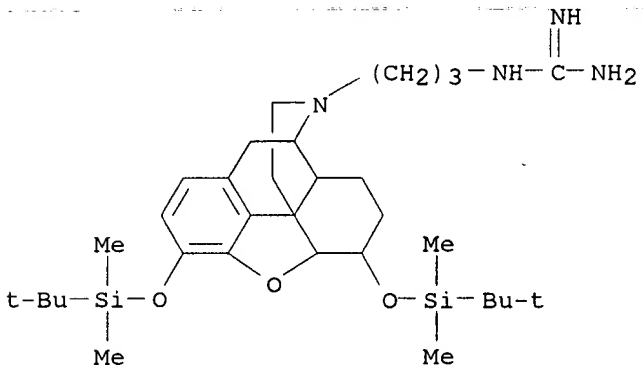


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     CM   2

     CRN  7664-93-9
     CMF  H2 O4 S
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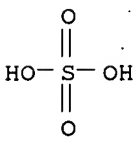


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             1 REFERENCES IN FILE CA (1967 TO DATE)
             1 REFERENCES IN FILE CAPLUS (1967 TO DATE)
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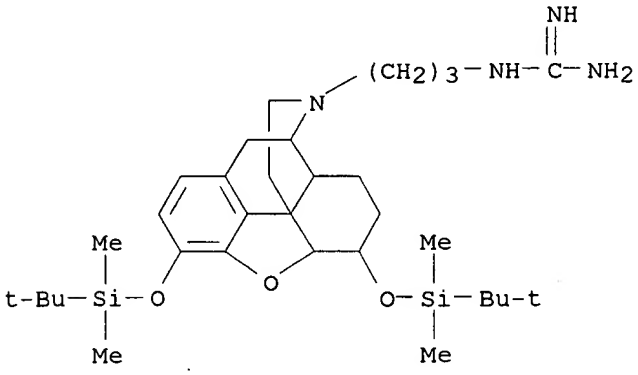
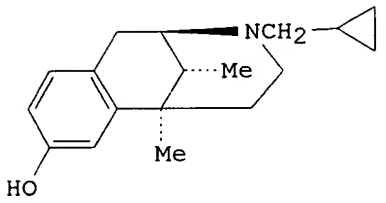
L1 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2001 ACS
RN **142740-96-3** REGISTRY
CN Guanidine, [(5.alpha.,6.alpha.)-3-[3,6-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,5-epoxymorphinan-17-yl]propyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Morphinan, guanidine deriv.
MF C32 H56 N4 O3 Si2
CI COM
SR CA
LC STN Files: CA, CAPLUS, TOXLIT



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L5 ANSWER 17 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1981:400113 CAPLUS
DN 95:113
TI Radioimmunoassay of cyclazocine and stereospecificity of antibody
AU Maeda, Masako; Tsuji, Akio
CS Sch. Pharm. Sci., Showa Univ., Tokyo, Japan
SO J. Pharmacobio-Dyn. (1981), 4(3), 167-74
CODEN: JOPHDQ; ISSN: 0386-846X
DT Journal
LA English
GI

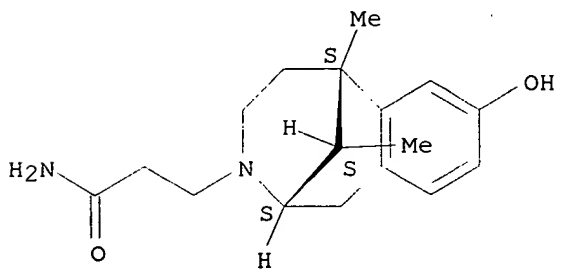


I

AB A new radioimmunoassay, using 3H-labeled dl-cyclazocine (I) [7346-09-0] rabbit antiserum and charcoal-dextran sepn. of bound and free cyclazocine, for the direct anal. of serum cyclazocine is described. This method, which is specific for cyclazocine and has a detection limit of .apprx.25 pg/assay tube, was successful in detg. the cyclazocine level in the sera of dogs injected i.m. with 3 or 10 .mu.g/kg cyclazocine. The drug half-life was 90 min; the apparent distribution vols. were 4.0 and 5.26 L/kg, resp. One of the antisera from rabbits immunized with dl-cyclazocin deriv.-bovine serum albumin conjugate was highly sp. for l-cyclazocine [7313-86-2].

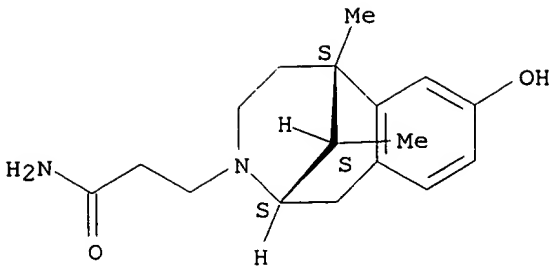
IT **77943-85-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, antibody formation in radioimmunoassay for cyclazocine in relation to)
RN 77943-85-2 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-propanamide, 1,4,5,6-tetrahydro-8-hydroxy-6,11-dimethyl-, (2.alpha.,6.alpha.,11R*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

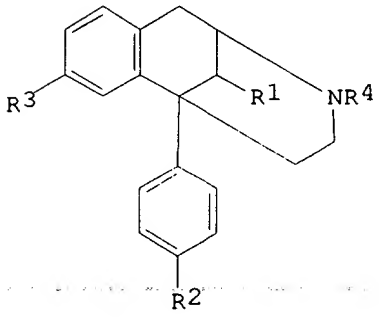


102(b)

1-5, 7, 23


Me
S
OH
H
Me
H2N
N
S
S
O
H

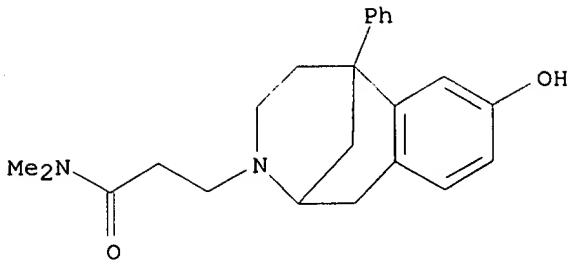
L5 ANSWER 19 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1979:432642 CAPLUS
DN 91:32642
TI Syntheses, analgetic activity and physical dependence capacity of 5-phenyl-6,7-benzomorphan derivatives
AU Yokoyama, Naokata; Almaula, Prabodh I.; Block, Fred B.; Granat, Frank R.; Gottfried, Norman; Hill, Ronald T.; McMahon, Elihu H.; Munch, Walter F.; Rachlin, Howard; et al.
CS Pharm. Div., Ciba-Geigy Corp., Ardsley, NY, USA
SO J. Med. Chem. (1979), 22(5), 537-53
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
GI



I

AB The title compds. I (R1 = H, Me, Et; R2 = H, Cl, F, OH, OAc; R3 = H, F, OH, Ac, OAc, OMe, etc.; R4 = H, CN, CO2Et, Me) were prepd. by generalized procedures from 4-piperidinones via Stevens rearrangement, followed by cyclization of the obtained product. The Stevens rearrangement products (4-aryl-2-benzyl-.DELTA.3-piperidine derivs.) and I were evaluated for analgesic effect and phys. dependence capacities in mice. The abs. configuration of I was established by comparison of their ORD and CD spectra of a known benzomorphan. Among the piperidine derivs. 2-benzyl-1-methyl-4-phenyl-.DELTA.3-piperidine-HBr [18136-06-6] and among I 1-2'-hydroxy-9.beta.-methyl-2-pentyl-5-phenyl-6,7-benzomorphan [70257-23-7] were the most potent analgesics. Structure-activity relations are discussed.

IT **70256-52-9P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and analgesic activity of)
RN 70256-52-9 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-propanamide, 1,4,5,6-tetrahydro-8-hydroxy-N,N-dimethyl-6-phenyl- (9CI) (CA INDEX NAME)



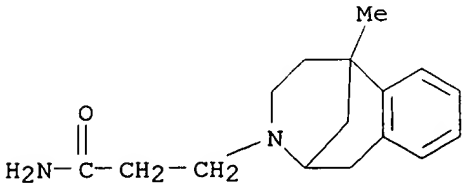
102(6)

1-5, 7, 18, 23-25

L5 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1975:43193 CAPLUS
DN 82:43193
TI Derivatives of 2-substituted-cyanoalkylbenzomorphane
IN Atsumi, Toshio; Kobayashi, Kenkji; Takebayashi, Yoshiaki; Yamamoto, Hisao
PA Sumitomo Chemical Co., Ltd.
SO Japan. Kokai, 6 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

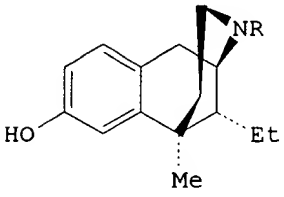
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 49072261	A2	19740712	JP 1972-116023	19721118

GI For diagram(s), see printed CA Issue.
AB I (R4-H, OH, lower alkoxy, alkanoyloxy, or reactive ester group; R1 = H, lower alkyl, alkoxyalkyl or aryl; R2, R3, and R4 = H, lower alkyl; R5 = reactive ester group) were treated with alkali cyanide to give I (R5 = CN), which were also prepd. by dehydration of I (R5 = CONH2). I (R5 = CN) are analgesics (no data). Thus, a mixt. of 2.5 g NaCN, 2.3 g 2'-tosyloxy-2-(.beta.-tosyloxyethyl)-5,9-dimethyl-6,7-benzomorphan and Me2SO was refluxed 8 hr. H2O added, and refluxed another 1 hr to give 0.4 g 2'-hydroxy-2-(.beta.-cyanoethyl)-5,9-dimethyl-6,7-benzomorphan. Also, a mixt. of 0.5 g 2-(.beta.-amidocarbonylethyl)-5-methyl-6,7-benzomorphan and 2.5 g POCl3 was refluxed 2 hr to give 0.2 g the corresponding 2-(.beta.-cyanoethyl)benzomorphan.
IT **54523-96-5**
RL: RCT (Reactant)
(dehydration of)
RN 54523-96-5 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-propanamide, 1,4,5,6-tetrahydro-6-methyl-(9CI) (CA INDEX NAME)

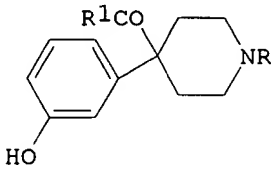


102(6)
1-5, 7, 18, 23-25

L5 ANSWER 18 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1979:449269 CAPLUS
DN 91:49269
TI N-(2-Cyanoethyl) derivatives of meperidine, ketobemidone, and a potent 6,7-benzomorphan
AU Uwaydah, Ibrahim M.; Waddle, M. Kathleen; Rogers, Michael E.
CS Med. Coll. Virginia, Virginia Commonwealth Univ., Richmond, VA, 23298, USA
SO J. Med. Chem. (1979), 22(7), 889-90
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
GI



I



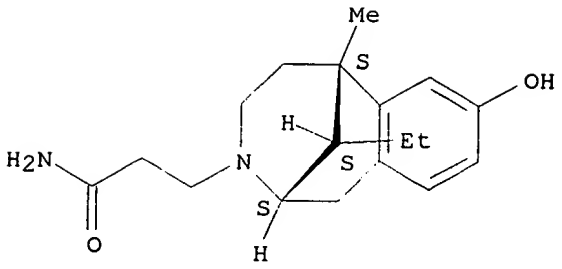
II

AB The cyanoethyl and carbamido derivs. of the benzomorphan I (R = CH2CH2CN, CH2CH2CONH2) and the cyanoethyl derivs. of meperidine and ketobemidone II (R CH2CH2CN; R1 = OEt, Et) were prepd. by alkylation of the resp. norbase with acrylonitrile and acrylamide and evaluated for analgesic activity in the hot-plate assay and for receptor affinity. 2-(2-Cyanoethyl)-9.alpha.-ethyl-2'-hydroxy-5-methyl-6,7-benzomorphan [70570-52-4] was 6 times more potent than its N-Me parent and showed a corresponding increase in receptor affinity; it did not show antagonistic activity in the tail-flick assay, and in single-dose suppression test substituted briefly for morphine. The activity of the N-2-cyanoethyl substituent is apparently dependent on the parent opiate. Structure activity relations are discussed.

IT **70650-78-1P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and analgesic activity of)
RN 70650-78-1 CAPLUS
CN 2,6-Methano-3-benzazocine-3(2H)-propanamide, 11-ethyl-1,4,5,6-tetrahydro-8-hydroxy-6-methyl-, (2.alpha.,6.alpha.,11R*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

102(6)
1-5, 7, 23
18, 24, 25


Me
S
OH
H
Et
H_2N
N
S
S
O
H

L5 ANSWER 8 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1994:280277 CAPLUS
DN 120:280277
TI Aminimide-containing molecules and materials as molecular recognition agents
IN Hogan, Joseph C., Jr.
PA Legomer Partners, L.P., USA
SO PCT Int. Appl., 128 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9401102	A1	19940120	WO 1993-US6241	19930630
	W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
				US 1992-906769	19920630
				US 1992-906770	19920630
				US 1993-41559	19930402
	AU 9346592	A1	19940131	AU 1993-46592	19930630
	AU 685752	B2	19980129		
				US 1992-906769	19920630
				US 1992-906770	19920630
				US 1993-41559	19930402
				WO 1993-US6241	19930630
	JP 08500339	T2	19960116	JP 1993-503400	19930630
				US 1992-906769	19920630
				US 1992-906770	19920630
				US 1993-41559	19930402
				WO 1993-US6241	19930630
	EP 723441	A1	19960731	EP 1993-916884	19930630
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
				US 1992-906769	19920630
				US 1992-906770	19920630
				US 1993-41559	19930402
				WO 1993-US6241	19930630
	BR 9306657	A	19981208	BR 1993-6657	19930630
				US 1992-906769	19920630
				US 1992-906770	19920630
				US 1993-41559	19930402
				WO 1993-US6241	19930630
	US 5705585	A	19980106	US 1995-204206	19950327
				WO 1993-US6241	19930630
	US 5981467	A	19991109	US 1996-765173	19960216
				US 1995-204206	19950327

AB The design and synthesis of novel aminimide-based mol. modules and the use of the modules in the construction of new mols. and fabricated materials are disclosed. The new mols. and fabricated materials are mol. recognition agents useful in the design and synthesis of drugs and have applications in sepns. and materials science. For example, 1,2-epoxydodecane is reacted with vincamine and 1,1-dimethylhydrazine to

give a conjugate, which is useful as a stabilization agent for the isolation and purifn. of receptor proteins which are therapeutically acted upon by vincamine and by structurally related mols.

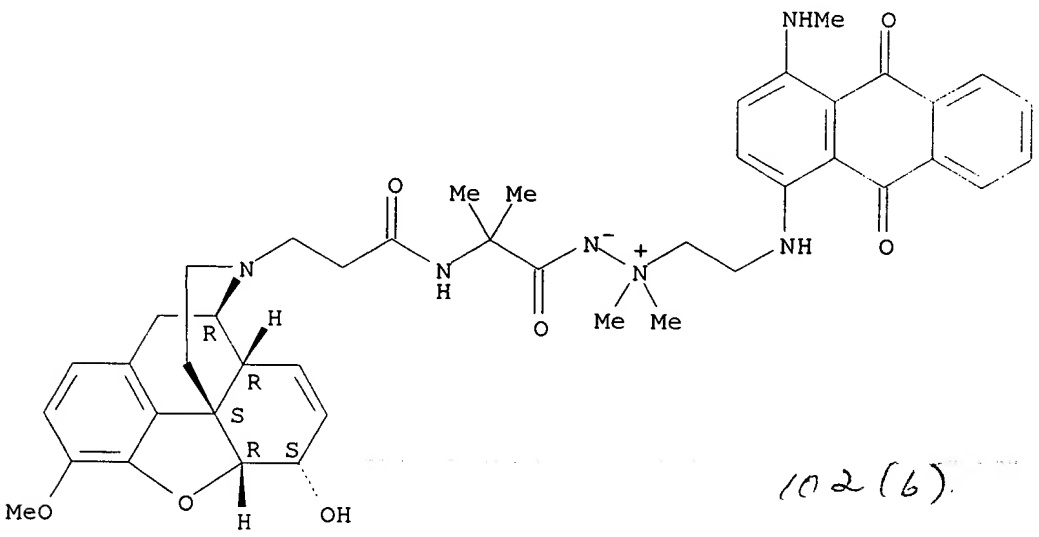
IT **154942-11-7P**

RL: PREP (Preparation)
(prepn. of, as probe for isolation of codeine-binding receptor proteins)

RN 154942-11-7 CAPLUS

CN Hydrazinium, 2-[2-[[3-[(5.alpha.,6.alpha.)-7,8-didehydro-4,5-epoxy-6-hydroxy-3-methoxymorphinan-17-yl]-1-oxopropyl]amino]-2-methyl-1-oxopropyl]-1-[2-[[9,10-dihydro-4-(methylamino)-9,10-dioxo-1-anthracenyl]amino]ethyl]-1,1-dimethyl-, inner salt (9CI) (CA INDEX NAME)

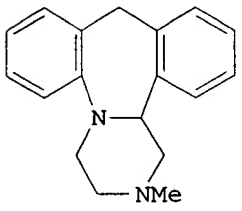
Absolute stereochemistry.



102(6).

1-4

L5 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2001 ACS
AN 1992:482892 CAPLUS
DN 117:82892
TI Chemical design of peripherally acting compounds
AU Jackson, W. Roy; Copp, Fred C.; Cullen, John D.; Guyett, Frances J.; Rae, Ian D.; Robinson, Andrea J.; Pothoulackis, Helen; Serelis, Algirdas K.; Wong, Margaret
CS Dep. Chem., Monash Univ., Melbourne, 3168, Australia
SO Clin. Exp. Pharmacol. Physiol. (1992), 19(1), 17-23
CODEN: CEXPB9; ISSN: 0305-1870
DT Journal
LA English
GI



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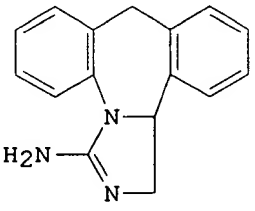
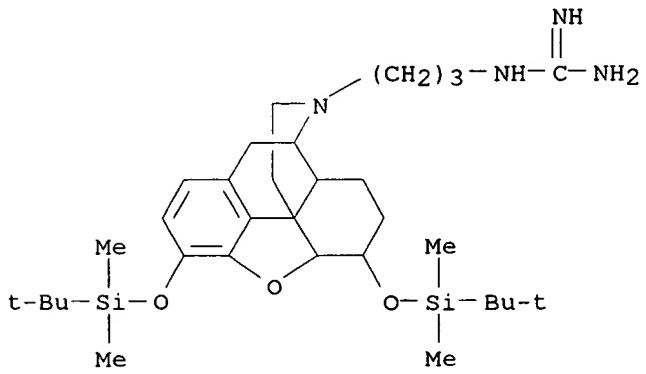


II

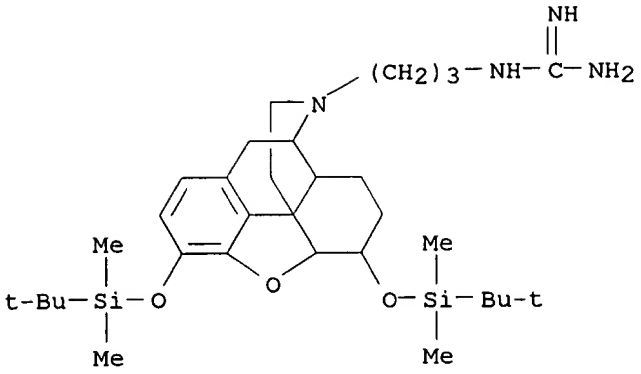
AB Some guanidines related in structure to mianserin (I) and WAL 801 (II) were synthesized and shown to be peripherally acting 5-HT2 antagonists. Structurally related compds. but not bearing a charged ionic group had central nervous system (CNS) activity. Computer-aided mol. modeling has been used to establish a 5-HT2 pharmacophore. The principle of exclusion from the CNS by incorporating a highly polar group to a biol. active mol. has been extended to the design and synthesis of a peripherally acting analgesic.

IT **142740-96-3P 142740-97-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and conversion to (aminoiminomethylaminopropyl)morphinan deriv.)

RN 142740-96-3 CAPLUS
CN Guanidine, [(5.alpha.,6.alpha.)-3-[3,6-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,5-epoxymorphinan-17-yl]propyl]- (9CI) (CA INDEX NAME)



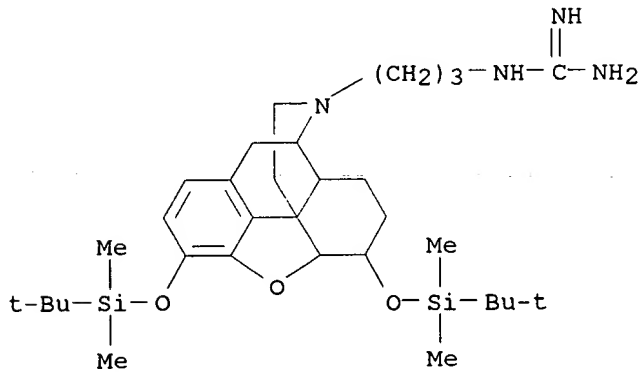
10 2(6).
cl 1-7 11-14, 17, 18
23-27



RN 142740-97-4 CAPLUS
CN Guanidine, [(5.alpha.,6.alpha.)-3-[3,6-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,5-epoxymorphinan-17-yl]propyl]-, sulfate (1:1) (9CI) (CA INDEX NAME)

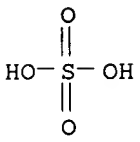
CM 1

CRN 142740-96-3
CMF C32 H56 N4 O3 Si2
CDES 4:5A,6A.MORPHINAN



CM 2

CRN 7664-93-9
CMF H2 O4 S



US 095820590EP1

Creation date: 01-16-2004
Indexing Officer: JLE1 - JESSICA LE
Team: OIPEBackFileIndexing
Dossier: 09582059

Legal Date: 08-13-2002

No.	Doccode	Number of pages
1	CTNF	9

Total number of pages: 9

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